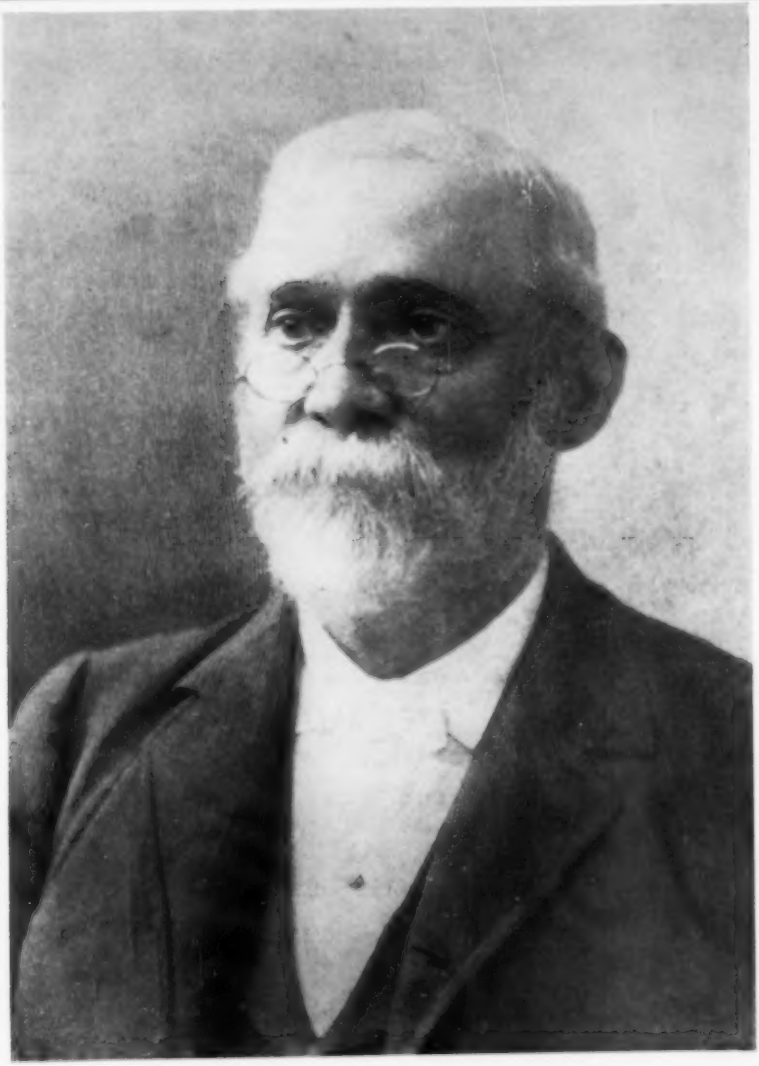
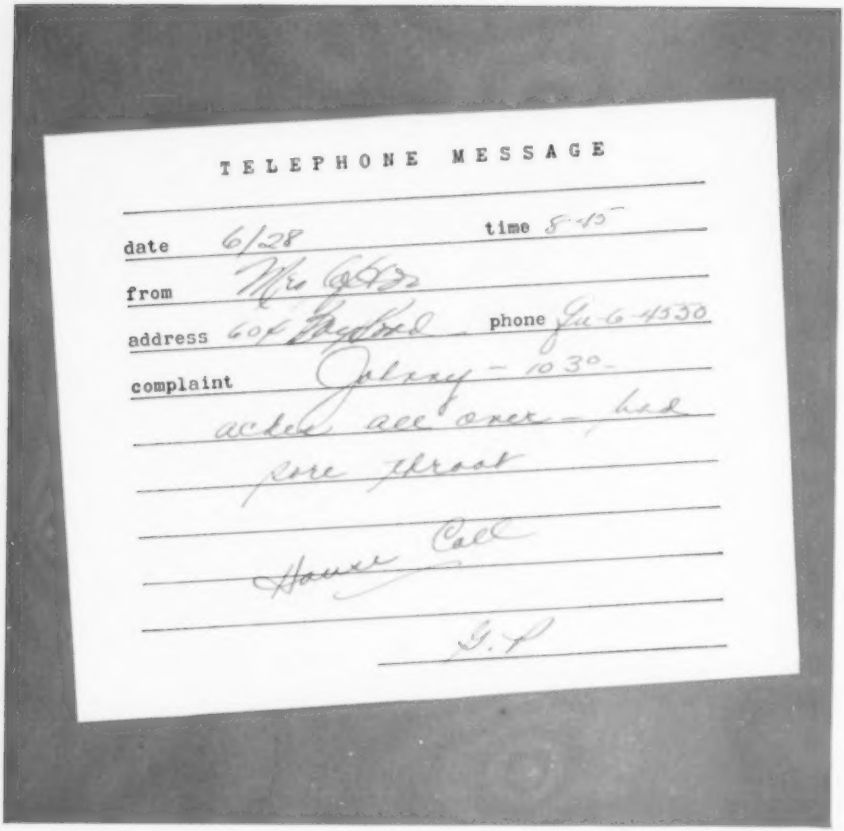
ARCHIVES OF PEDIATRICS

August 1959



Pioneers of Pediatrics . . . Job Lewis Smith (1828-1897)



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1. Perkins, J. L.: Kansas State M. J. (to be published).

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Albro C. Gaylor, Publisher

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Vol. 76, No. 8

August 1959

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THE TRANQUILIZER UNIQUE IN PEDIATRICS

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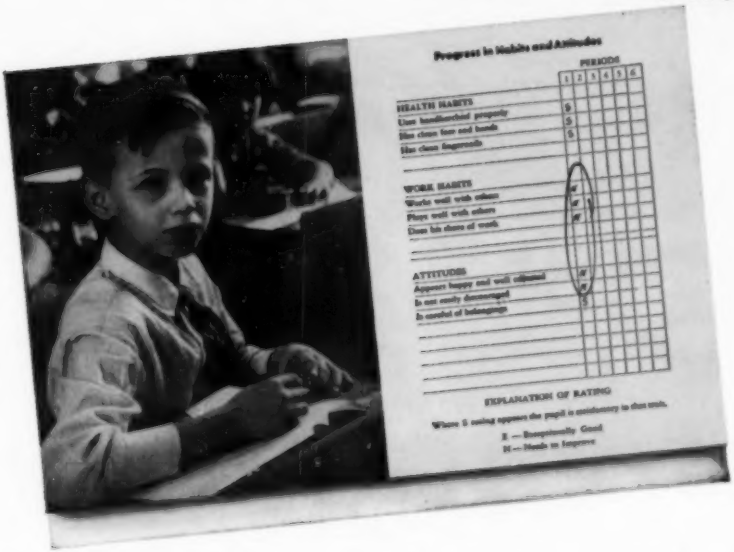

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References: 1. Nathan, L. A., and Andelman, B. M.: Illinois M. J. *112*:171 (Oct.) 1957. 2. Bayart, J.: Presented at International Congress of Pediatrics, Copenhagen, Denmark, July 22-27, 1956. 3. Ayd, F. J., Jr.: California Med. *87*:75 (Aug.) 1957.

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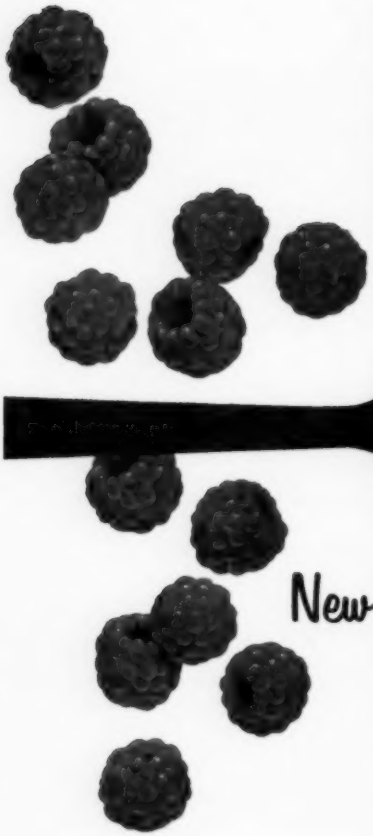
The Cover-Job Lewis Smith (1828-1897) (© "Pioneers of Pediatrics")

Dr. Job Lewis Smith, one of this country's first physicians to devote his major practice to pediatrics, was surpassed in his influence on American pediatrics only by Dr. Jacobi. It has been said that the distinction "Father of American Pediatrics" would otherwise have been Dr. Smith's. Professor of clinical pediatrics at the Bellevue Hospital Medical College, and attending physician to several hospitals . . . he still had time to contribute much thru writing. His book "A Treatise on Disease of Infancy and Childhood" saw eight editions between 1869 and 1896.



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August 1959
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TUBERCULOSIS IN CHILDHOOD

Part IV

REGRESSIVE PULMONARY INFILTRATES OF TUBERCULOUS ORIGIN ("EPITUBERCULOSIS")

Ph. SCHWARTZ, M.D.*

Pennsylvania

IV. MORPHOLOGY AND PATHOGENESIS OF THE REVERSIBLE INFLAMMATORY INFILTRATIONS IN HUMAN PATHOLOGY

The two—predominantly cellular or predominantly necrotic—types of reversible pulmonary infiltrations, induced by tubercle bacilli in our experiments, occur also in man. Although, in principle, no morphological differences exist between them, and both develop under similar pathogenetic conditions, having been caused by the same event—namely, by the lymphonodo-bronchogenic superinfection in the initial period of pulmonary tuberculosis—we find it useful to consider separately the two forms of reversible pulmonary condensations in human pathology. This procedure accords better with the historic development, which necessitates the confirmation of a number of controversial findings; also, it conforms more closely with the predominating clinical attitude, which discriminates between "epituberculous" and "genuine" tuberculous processes.

a. *Predominantly Cellular, Reversible Chronic Pneumonic Processes in Human Pathology*

Based on the study of 10 instances—children and adults (Group II)—in whom extensive, mostly lobar involvements were present, we were able to observe that the reversible, chronic pneumonia characterized macroscopically by a rubber-eraser-like consistency

* Chief, Dept. of Pathology, Warren State Hospital, Warren, Pa.; Prof. of Gen. Path. and Path. Anat., Univ. Frankfurt-M., Germany; Former Director, Dept. Path. at the Univ. Istanbul, Turkey.

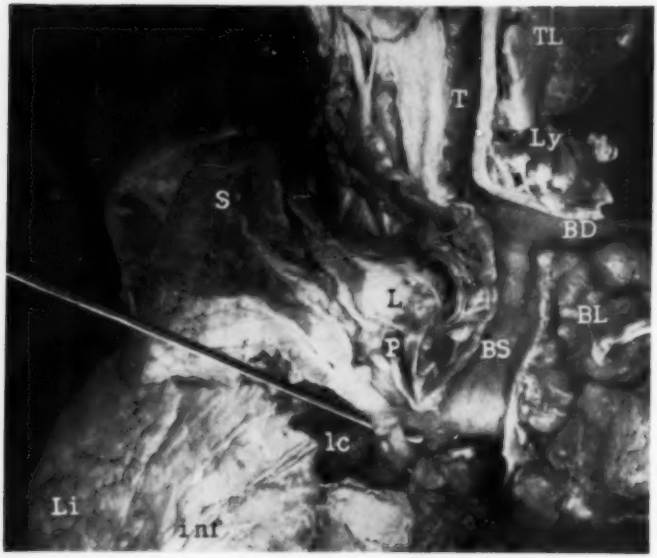

Fig. 5. Extensive, Massive, Rubber-Eraser-Like Aspiration-Infiltration of the Lingula, Caused by Discharge of Tuberculous Lymph Nodes into the Bronchial System. (Five-year-old girl; A. 941/46, Istanbul; Group II, Case No. 4).

Probe . . . . leads through the lymph-node cavity and the orifice of the lingular bronchus.

lc—lymphnode cavity.
inf—aspiration-infiltration.

of the infiltrated pulmonary areas (Fig. 4, Arch. Ped., Vol. 74, p. 167 and Figs. 5, 6, 7, 8, 9) and microscopically by intra-alveolar cellular infiltrations, corresponds in every respect to changes we encountered in animal experiments. (Fig. 7, Arch. Ped., Vol. 75, p. 324) and Figs. 7, 9 of the present paper). In relation to the pathogenesis, it is important to stress that the pulmonary condensation appeared in patients approximately 4 to 8 weeks after the onset of the infection, i.e., at a time when our experimental animals were most susceptible to inflammatory reactions. The decisive importance of hypersensitivity in human pathology is indicated by the fact that extensive epituberculous pulmonary infiltrations develop very quickly. In our experiments, in which intravenous superinfections were administered, we interpreted the absence of notable necroses and the reversibility of the inflammation, in general, as a result of the presence of an effective immunity. Corre-

spondingly, we assume that in human pathology the development of reversible chronic pneumonic infiltrations also indicates the prevalence of an acquired defensive ability. From an etiological viewpoint, the parallelism is striking: The large reversible infiltration develops in both groups directly after a massive superinfection—in

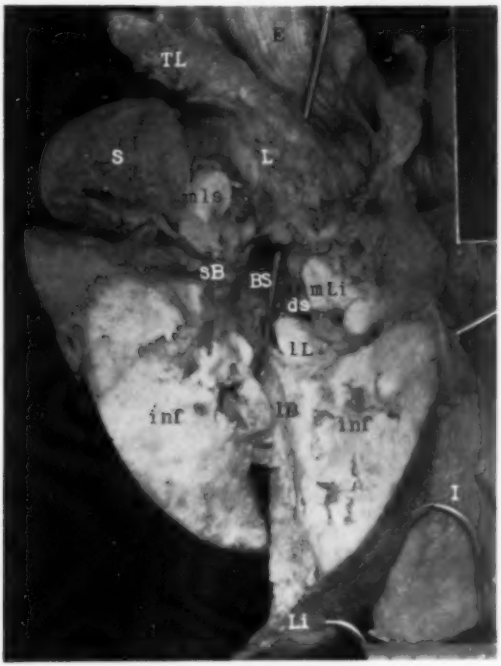

Fig. 6. Massive Rubber-Eraser-Like Aspiration-Infiltration Caused by the Discharge of Large Tuberculous Lymph Nodes into the Main Bronchus of the Left Lung. (Case No. 1 of Group II; 8-month-old boy; A. 348/47, Istanbul).
inf—aspiration-infiltrate of the lingula.

our animal experiments resulting from a single intravenous or intratracheal injection; in human pathology, following the spontaneous penetration and discharge of necrotic lymph nodes into the bronchial system—sometimes occurring repeatedly in rapid succession.

We observed, in spontaneous involvements of human pathology as well as in animal experiments, the same forms of infiltrations, permitting the definition of three typical developmental stages:

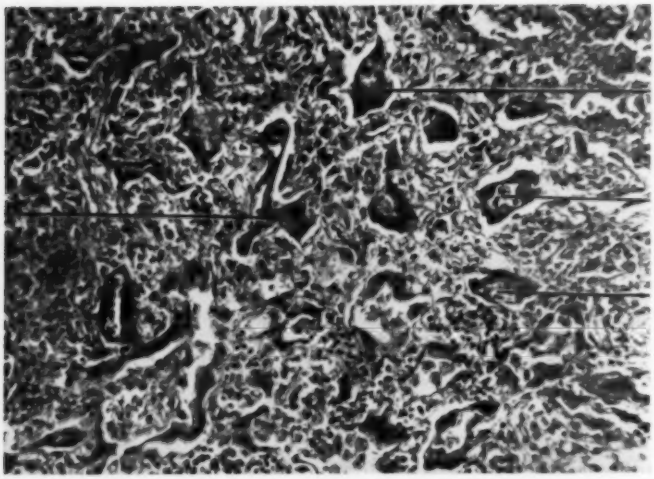

Fig. 7. Microscopical Aspect of the Lingular Aspiration-Infiltrate Demonstrated in Fig. 6.
Probes . . . . indicate very large, syncytial giant cells, which were excessively filled with tubercle bacilli.
The microscopical changes of this observation are characteristic of the initial, proliferative stage of a lymphonodogenic, rubber-eraser-like, regressive, chronic pneumonia.

1. *Proliferative stage,* in which the lively multiplication of alveolar cells predominates, producing massive intra-alveolar cell conglomerates and syncytial giant cells (Fig. 7). These changes are characteristic of the first two to three weeks subsequent to the second experimental treatment, or to the endogenous lymphonodobronchogenic superinfection.

2. *Stage of consolidation,* in which the syncytial cell groups disintegrate and the alveolar cells form epithelium-like seams; of the earlier, very numerous giant cells, only a few typical Langhans-elements remain. The disintegration and decay of the intra-alveolar infiltrates begins (Fig. 9).

The period of consolidation does not prevail for long—it starts approximately in the third week after the superinfection and persists only 6 to 10 weeks more.

3. *Stage of healing,* in which the regression of the infiltration predominates, characterized by the dissolution of individual cells in the infiltrate, or by the necrosis of whole groups of intra-alveolar elements. In areas in which the infiltrate cannot be eliminated or digested without destroying parts of the pulmonary structure,

tubercle-like conglomerates develop and diffuse granulation processes occur. Later, tubercles become subjected to hyalinization and to a progressive loosening. Depending on the extension of these processes, the stage of healing may be prolonged for many months (Fig. 10).

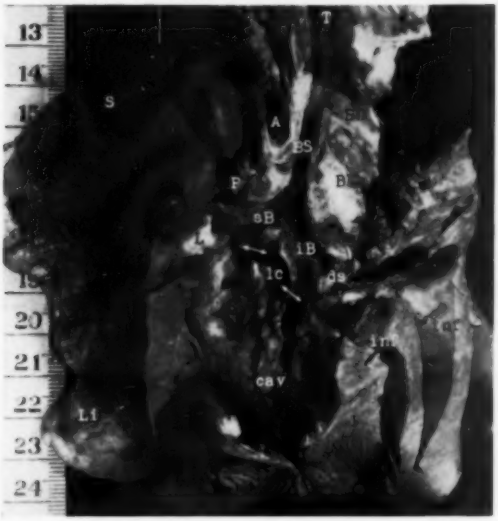

Fig. 8. Cavitated Rubber-Eraser-Like Infiltrate of the Left Lower Lobe Caused by Discharge of Tuberculous Lymph Nodes of the Lateral-Interlobar Space into the Main Bronchus of the Left Lower Lobe, and into the Lingular Bronchus. (Case No. 9 of Group II; 1½-year-old male; A. 739/47, Istanbul).
The entire left lower lobe was massively infiltrated. The cavity occupied the sector supplied by the axillary bronchus of the left lower lobe.
lc—lymph-node cavity of the lateral interlober space. *Superior arrow* shows the perforative defect connecting the lymph-node cavity with the lingular bronchus. *Inferior arrow* indicates the defect leading from the lymph-node cavity into the lower-lobe main bronchus.
cav—cavity of the left lower lobe.
inf —massive rubber-eraser-like infiltrate of the left lower lobe.

Thus, we feel justified in considering the chronic reversible pneumonia in human pathology to be also an *infiltration produced by superinfection*. It develops in the initial period of pulmonary tuberculosis, when the highest point of sensivity is reached and simultaneously a forceful immunity becomes effective, subsequent to the aspiration of necrotic tuberculous lymph nodes discharging into the tracheobronchial system. Very extensive rubber-eraser-like pneumonic infiltrations develop in both children and adults,

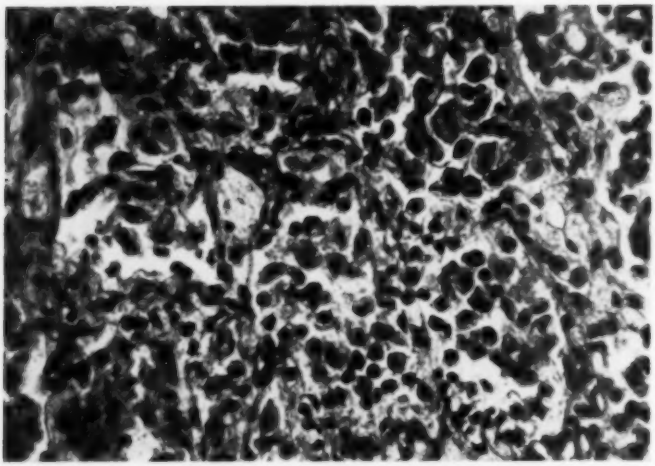

Fig. 9. Microscopical Aspect of the Rubber-Eraser-Like Infiltration Displayed in Fig. 8.

Alveolar histiocytes predominate. The cells contained only very few tubercle bacilli.

This observation is characteristic of the consolidation stage of a lymphonodogenic, rubber-eraser-like, regressive, chronic pneumonia.

and may follow similar courses. The impression gained by clinical observations, that reversible (epituberculous) infiltrates occur more frequently in children than in adults, may be explained, perhaps, by the fact that a lobar involvement in children is a relatively more severe condition than in adults. Also, the family and community, in general, are concerned more for children than for adults. Therefore, a benign pulmonary infiltration in a child has a better chance of being discovered. In respect to the relatively greater number of pathologic-anatomical observations relative to rubber-eraser-like pulmonary condensations in children, the following facts may be of importance: Small children, being more frail, are more endangered by tuberculous meningitis and by intercurrent infections.

We repeatedly had the opportunity to investigate rubber-eraser-like pneumonic infiltrations in adults affected by chronic pulmonary tuberculosis and subject to relapses of this disease. In these cases, too, the pulmonary condensations were induced by the penetration and discharge of tuberculous lymph nodes into the bronchi during the period in which high inflammatory disposition (hypersensitivity) and immunity occurred together. However, reversible

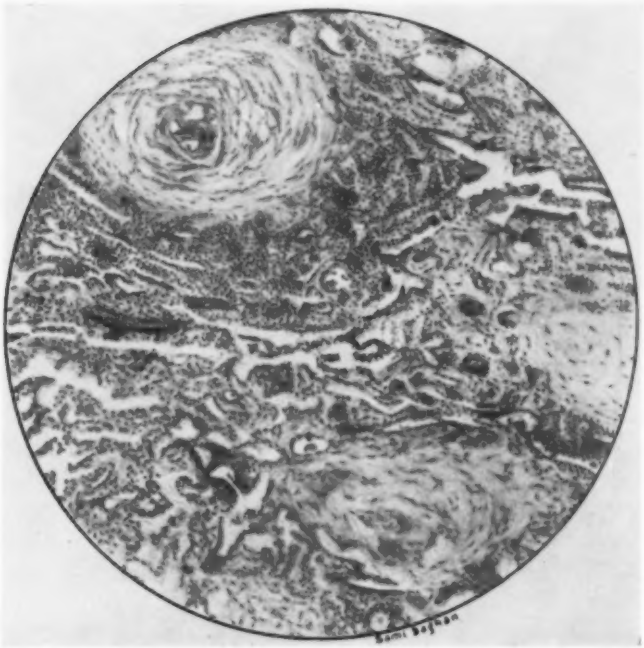

Fig. 10. Microscopical Aspect of Advanced Stage of Healing of a Rubber-Eraser-Like Aspiration-Infiltration. (Case No. 5 of Group III; 6-year-old boy; A. 885/47).

The picture shows three, almost completely hyalinized tubercles, chronic inflammatory infiltration and atelectatic collapse. These changes were observed in a case in which lymphonodogenic caseous aspiration-infiltration predominated.

rubber-eraser-like pneumonic infiltrations—sometimes involving all parts of both lungs—are possibly also caused by hematogenous spread. (See Fig. 6 of our second publication of this series, Arch. Ped. Vol. 75, p. 463).

In some instances of typical rubber-eraser-like pneumonia, we observed more or less extensive cavities, caused by dissolution processes, manifestly occurring shortly before death (Group II, Cases 8, 9 and 10). No zone of demarcation, no "pyogen" membrane was present between the cavity and the surrounding pneumonic condensation. The number of tubercle bacilli was extremely reduced, just as in comparable cases of a massive macrocellular pneumonia. We consider the cavitation to be the consequence of

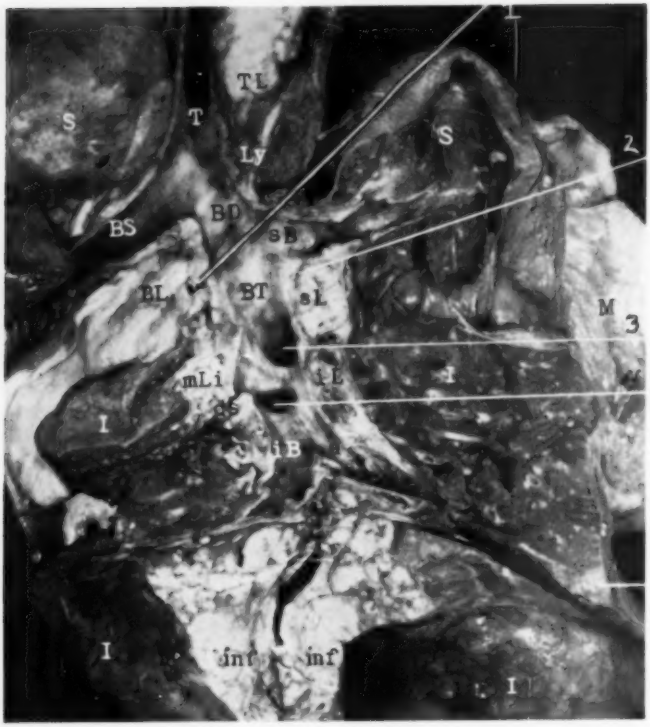

Fig. 11. Massive Caseous Infiltration. Large Cavity of the Right Lower Lobe, Following Multiple Extensive Lymphonodogenic Lesions of the Bronchial System. (Case No. 6 of Group III; 3-year-old girl; A. 32/48, Istanbul).
Probe 1 .... indicates the perforative defect of the right stem-bronchus, leading into the extremely enlarged and almost completely emptied caseous bifurcation lymph nodes.
Probe 2 .... indicates the transitional area between right stem-bronchus and main bronchus of the upper lobe, penetrated by caseous lymph nodes of the superior interlobar space.
Probe 3. .... indicates the orifice of the main bronchus of the middle lobe, which was severely damaged by surrounding tuberculous lymph nodes.
Probe 4 .... indicates the orifice of the median bronchus, which was mutilated by tuberculous lymph nodes located between the main bronchus of the lower lobe and the main bronchus of the middle lobe.
inf—massive caseous aspiration-infiltration affecting the dorsal-basal part of the right lower lobe.

an intercurrent influence, inducing necrosis and disintegration by sudden and permanent interruption of the prestasic circulatory retardation, which prevailed for a very long duration in the condensed pulmonary area.

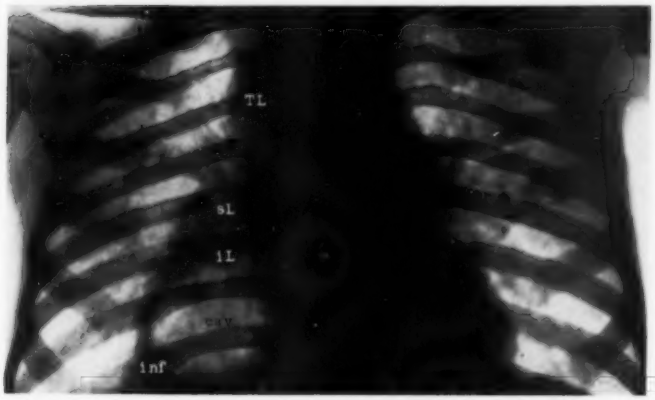

Fig. 12. Radiography Taken Three Days before Death—(Case No. 6 of Group III; 3-year-old girl; A. 32/48, Istanbul).
TL..... Large paratracheal, partially caseous lymph-node complex, visible in photograph of this case. (See Fig. 11, *TL and Lx.*)
sL..... Caseous lymph-node complex of the superior interlobar space (visible in photograph, sL).
iL..... Lymphnode situated in the inferior-lateral interlobar space of right lung (visible in photograph, iL).
cav.... Large cavity of the sector supplied by the median bronchus. At autopsy, the median bronchus was found mutilated by large tuberculous lymph nodes connected with lymph nodes of the inferior, lateral, interlobar space).
inf..... Part of the caseous infiltrate involving the basis of the right lower lobe, visible in the photograph (Fig. 11:I).

b. *Caseous Reversible Pulmonary Infiltrates in Human Pathology.* (Fig. 5, in Arch. Ped., Vol. 74, p. 169 and Figs. 11, 12, 13, 14 of the present paper).

A few instances of regressing, or healed epitubercular pulmonary infiltrates were described, in which post-mortem examination disclosed the presence of extensive, massive necroses (Oppenheimer, Haferkorn-Goeters, Rössle, Fish-Pagel). In comparing these findings with changes in sensitized animals, subjected to intratracheal superinfections, it is impossible not to notice basic similarities. Thus, we confirm the assumption, often voiced, that this type of infiltration in human pathology also represents lesions which are the result of particular conditions.

We have had the opportunity of investigating relatively large numbers of cases of this type, defining their morphological, pathogenic and etiologic peculiarities (Group III). We found that between infiltrates of this group, and chronic pneumonia characterized by rubber-eraser-like consistency, only quantitative differences

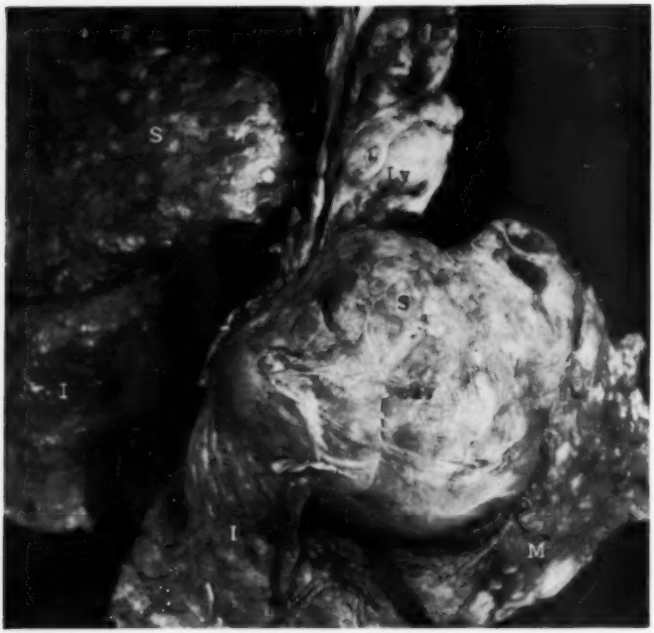

Fig. 13. Giant Cavity of the Right Upper Lobe Developed Following Disintegration and Dissolution of Extensive Lymphonodogenic Caseous Bronchial Lesion (Case 7 of Group 3; 1½-year-old girl; A. 3/48, Istanbul).
cav .... cavity of the right upper lobe. The left lung and the right middle and lower lobes displayed numerous, quite large miliary tubercles.

were present: Necroses, which in moderate extension often accompany fresh rubber-like pneumonic processes, predominate in these cases, distinguished by a caseous consistency of the pulmonary condensation; on the other hand, cicatrices and defects, remaining after the regression of the initial caseous infiltration, are, even if of greater extension, similar to cicatricial sequelae of a typical rubber-eraser-like pneumonia. From a pathogenic and etiological viewpoint, there are no differences at all. Both the rubber-eraser-like pneumonic infiltrates and the reversible caseous pulmonary infiltration result from the aspiration of infectious and toxic masses discharged by necrotic tubercular lymph nodes from the bronchial system 4 to 8 weeks after an exogenous infection, or during the initial period of a reactivation process. This is the decisive criterion: all changes developing immediately following lymphonodo-bronchogenic superinfections, in a typical interval

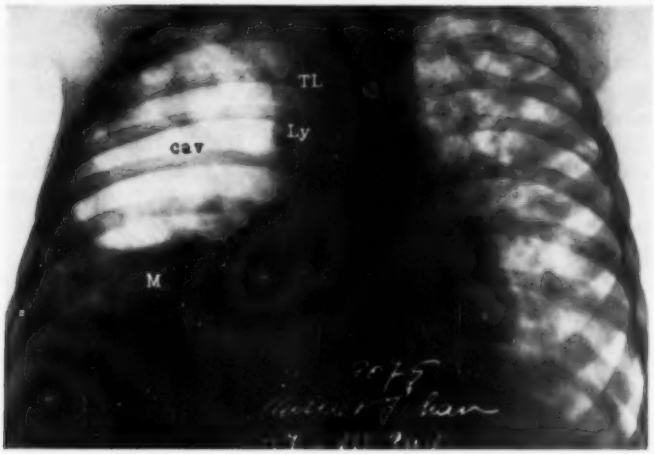

Fig. 14. Radiography of the Case Demonstrated in Fig. 13.
cav .... Large cavity of the right upper lobe.
TL ..... Large paratracheal lymph node (which is visible in the photograph, Fig. 13, TL).
Ly ..... Paratracheal tuberculous lymph node located below the right subclavian artery (This lymph node is visible in the photograph, Fig. 13, Ly.).

after the onset of a primary infection or of a disease initiated by a reactivation, are reversible and, a priori, benign. As in analogous animal experiments, they reach the highest point of their development in a relatively short time—a few weeks—after the occurrence of the massive superinfection. It is then that all the specific attributes of a tuberculous disease begin to disappear in consequence of a characteristic healing process, sometimes extending over a period of many years. *Appearance in the initial period of pulmonary tuberculosis, involvement of extensive pulmonary parts, cessation of progress after the complete discharge, or obliteration of the lymph-node cavities, healing processes continuing for years, the formation of extensive cicatrices: these are the characteristics of regressive pulmonary disease initiated by caseous infiltrates.*

As to the pathogenesis of predominantly caseous lymphonodogenic aspiration-infiltrations, let us emphasize that here the quantity of the discharged necrotic and disintegrated lymph-node masses evidently is of decisive importance. In all our corresponding cases, particularly voluminous lymphonodogenic bronchial defects were present, concordant with the participation of excessively

large lymph-node complexes (Fig. 5, in Arch. Ped., Vol. 74, p. 169 and Figs. 11 and 13 of the present publication). It is permissible to assume, therefore, that we deal in these cases with similar occurrences as in experiments in which pre-infected animals received particularly large doses of an intratracheal superinfection (see Fig. 5, Fig. 6 in Arch. Ped., Vol. 75, p. 322 and 323); by a massive lymph-node discharge into the bronchial system, a preinflammatory prestasic circulatory stagnation, involving an extensive pulmonary area, was subjected to a definitive or prolonged interruption.

GROUP II

MASSIVE AND CAVITATED RUBBER-ERASER-LIKE, LYMPHONODO-BRONCHOGENIC PULMONARY INFILTRATES

Case No. 1. (Figs. 6 and 7) The autopsy (No. 348/47, Istanbul) of an eight-month-old boy, who died of miliary tuberculosis and tuberculous meningitis, disclosed extremely enlarged paratracheal as well as parabronchial lymph nodes, bilaterally, transformed into giant lymph-node cavities. Lymph nodes of both lungs were intensely enlarged, affected by caseous tuberculosis. Large lymphonodogenic perforative defects of the left main bronchus, of the main bronchus of the left upper lobe and of the esophagus were present. A massive, homogeneous, lobar infiltration of rubber-eraser-like consistency gave the lingular segment of the left upper lobe the aspect of an independent organ. A fine, hematogenic dissemination pervaded both lungs. Microscopic examination disclosed the proliferative stage of a pulmonary infiltration induced by massive superinfection at the climax of inflammatory susceptibility (hypersensitivity): predominantly intra-alveolar, macrocellular infiltration; few necroses; very numerous, particularly large giant cells; no tubercles (Fig. 7). Extensive polymorphonuclear, intra-alveolar infiltration (acute, common pneumonia) also was present. Alveolar cells contained an extraordinarily high number of tubercle bacilli, giant cells, and polymorphonuclear leucocytes. In some microscopic fields, as many as 4500 germs were counted! (Immersion obj. 105 x; oc. 12 x) Assumedly, the tubercular infection and the lymphonodogenic bronchial (and esophageal) lesions occurred 2-3 months and 2 to 4 weeks, respectively, before death.

A radiograph taken two days before death revealed enlarged lymph nodes, lymph-node cavities, and extensive pulmonary condensation of the left middle field. The radiographic aspect of the pulmonary condensation conformed perfectly to changes which were described as typical "epituberculosis."

Remarks: No primary focus was observed. We assume that it was hidden within the extensive aspiration-infiltration of the lingula.

Epicrisis: This is a typical case of fresh primary tuberculosis, characterized by lymphonodogenic aspiration-infiltration. In spite of the extraordinary amount of tubercular bacilli within the lungs, the inflammatory reaction, following the discharge of tuberculous lymph nodes into the bronchial system, was mild, producing no necroses. We assume that the inflammatory faculties of the microbes were inhibited by the effect of immune bodies. We regard the lobar extension of the aspiration-infiltration as due to the highly increased inflammatory disposition which prevailed at the time of the lymphonodobronchogenic spread. The accumulation of tubercle bacilli in the aspiration-infiltration of the left upper lobe signifies the effect of an inflammatory fixation-phenomenon.

Case No. 2. A 2½-year-old girl suffered for approximately three months from respiratory paroxysms, considered whooping cough. One day before death, fever appeared, accompanied by vomiting, diarrhea and by a rash

which seemed to indicate scarlet fever. Sudden deterioration and cramps ended fatally. Tuberculous pulmonary changes following fresh primary infection, observed at autopsy (No. 502/29, Frankfurt-Main), seemed insufficient to explain this case. Up to cherry-sized tuberculous lymph nodes filled the bifurcation space, and the lateral and mediodorsal interlobar spaces of the left lung; paratracheal lymph nodes were affected by tuberculosis bilaterally; caseous areas in lymph nodes did not predominate. We observed lymphonodogenic, tubercular penetration foci of microscopic size in numerous bronchi of the left upper lobe. The lingula contained a bean-sized, irregularly limited, massive, grayish-pink condensation, located in the sector of the bronchi displaying lymphonodogenic penetration. A cherry-stone-sized, roundish primary focus, located subpleurally in the basis of the lower lobe, was surrounded by a loose, quite extensive perifocal infiltrate. A fine hematogenic dissemination affected both lungs. Microscopic examination of the condensation disclosed macrocellular infiltration with numerous, large giant cells: the beginning proliferative stage of an allergic pneumonia caused by tubercular superinfection; no necroses and no tubercular structures were present! Duration of the tubercular infection was assumed to be *2½-3* months; we believe that the lymphonodogenic penetration of the bronchi and consecutive bronchial spread began *3* to 5 weeks before death.

No clinical radiography was available.

Remarks: The cutaneous rash, observed shortly before death, probably was the consequence of a hematogenic dissemination. The whooping cough-like episodes were perhaps caused by the enlarged tubercular parapulmonary lymph nodes.

Epicrisis: This is one of the few instances in our material, in which lymphonodogenic aspiration-infiltrates without necrotic processes were observed. We assume that the development of the lymphonodogenic aspiration-infiltration was in its initial stage, not only in respect to its quality but also in regard to its extension.

Case No. 3. The autopsy (No. 237/47, Istanbul) of a ten-month-old male disclosed moderate swelling and caseous tuberculosis of paratracheal lymph nodes bilaterally; swelling and caseous tuberculosis of the bifurcation space. The lymph nodes of the superior, inferior lateral and mediodorsal interlobar spaces, as well as the lymph nodes of the hilum angles of the right lung, also were involved; while interbronchial lymph nodes of the left lung showed no participation! A pea-sized, completely emptied and almost clean lymph-node cavity of the main bronchus of the lower lobe was located immediately below the orifice of the middle-lobe bronchus; very numerous penetration foci (mucosal erosions!) affected the right stem bronchus, at the level of numerous, large caseous lymph nodes of the inferior hilum angle. A massive, homogeneous, lobar infiltration of elastic, rubber-eraser-like consistency pervaded the right middle lobe, hiding a typical cherry-stone-sized, concentrically stratified primary focus (See Fig. 4, in Vol. 74, p. 167, Arch. Pediatrics). A fine hematogenic dissemination was present in both lungs. Microscopic examination of the middle-lobe condensation showed a predominantly macrocellular intra-alveolar infiltration (subchronic stage of "desquamative" pneumonia; stage of consolidation, in transition to early stage of healing); marked loosening of the intra-alveolar infiltration; restricted necrotic areas; sparsely scattered tubercles; few giant cells, all of Langhans-type; and hyaline transformation of necroses (similar to the observation illustrated with Fig. 10). An average of 10-15 tubercle bacilli was found in each microscopic field of the desquamative pneumonia (intra- and extracellularly located); in necrotic (caseous pneumonic) areas: averaging 100 germs in a microscopic field; in tubercles: an average of 10-20 bacilli (located in the central necroses and in epithelioid cells). We believe that the tubercular infection occurred 4-5 months and the lymphonodogenic discharge into the bronchial system *2* to *3* months before death.

No clinical radiography was present.

Remarks: The lymphododogenic superinfection originated from the lymph-node cavity as well as from the numerous mucosal erosions of the right stem bronchus.

Epicrisis: We consider the lobar extension of the aspiration-infiltration to be the expression of the hypersensitivity prevailing at the time of the lymphonodo-bronchogenic spread. The reduced number of tubercle bacilli observed within the aspiration-infiltration is due to the destructive effect of immune substances.

Case No. 4 (Fig. 5) The autopsy (No. 941/46, Istanbul) of a five-year-old girl disclosed, bilaterally, considerably enlarged paratracheal tuberculous caseous lymph nodes; filling of the bifurcation space as well as the lateral and mediodorsal interlobar spaces of the left lung with large, caseotuberculous lymph-node complexes; enlargement and caseotuberculous infiltration of intrapulmonary—interbronchial—lymph nodes of the left upper lobe; enlargement and tuberculous involvement of numerous lymph nodes of the *right* lung. An extensive destruction of the proximal part of the lingular bronchus, connected with a cherry-sized parabronchial lymph-node cavity, was caused by discharging disintegrated tuberculous lymph nodes of the lateral interlobar space of the left lung. This lymphonodogenic bronchial lesion was accompanied by a massive, homogeneous lobar aspiration-infiltration of rubber-eraser-like consistency of the lingular segment; no primary focus was found. Microscopic examination of the lingular condensation revealed a predominantly intra-alveolar, macrocellular infiltration with relatively few and small necrotic centers; lymphocytes; plasma cells; a few giant cells of Langhans' type: extensive arterial thromboses of the condensed areas, accompanied by hemorrhagic infiltrations; no tubercles! Thus, we dealt in this case with the early consolidation stage of an allergic pulmonary infiltration induced by lymphonodogenic aspiration infection. Necrotic (caseous pneumonic) areas contained sparsely disseminated tubercle bacilli: 12-46 in one microscopic field (Imm. obj. 105x; oc. x); in areas characterized by intra-alveolar macrocellular infiltrations, bacilli were mostly included in alveolar cells (30-76 per field), the number of germs in individual elements being very low (2-10). Individual giant cells contained either only 1-2 tubercle bacilli or none at all! The age of the tubercular infection was approximately 3 to 5 months; we assume that the discharge of tuberculous lymph nodes into the bronchial system occurred 2½ to 3½ months before death.

No radiography was present.

Remarks: The massive lobar infiltration of the lingula developed consequent to the discharge of disintegrated tuberculous lymph nodes into the lingular bronchus.

Epicrisis: The discharge of the necrotic lymph-node masses into the bronchial system occurred in a stage of the disease in which the pulmonary inflammatory susceptibility was at its acme; concurrently, a strong postinfectious immunity prevailed. The lobar extension of the aspiration-infiltration evidences the hypersensitivity of the affected pulmonary tissue. The low number of tubercle bacilli indicates the destructive and inhibitory effect of a strong immunity.

Case No. 5. A 37-year-old woman died of sepsis, purulent pyelonephritis and multiple sclerosis. Autopsy (No. 36/54, Warren) disclosed an old bean-sized, very hard focus of the lingular tip; old calcified scar of the right middle lobe, and the following changes due to a post-primary lymphonodogenic reactivation: fresh caseous tuberculosis and moderate swelling of the lymph nodes of the left lung; a narrow anthraco-tuberculous, perforative lesion located just below the orifices of the dorso-paravertebral, the ant. oblique bronchus and the common opening of the axillopectoral system of the main bronchi of the left upper lobe, and produced by the discharge of a tuberculous lymph node of the superior hilum angle. The fresh perforation occurred in the area of a rather old perforative scar! An extensive, massive, homogeneous, rubber-eraser-like infiltration affected the sectors of the left upper lobe, aerated by the dorsal horizontal, the post. oblique, the ant. oblique bronchi and by the axillopectoral system; similar, scattered, lobular pneumonic infiltrates were present also in the right lower lobe. Microscopic examination disclosed the consolidation stage of an allergic aspiration-infiltration of lymphonodo-bronchogenic origin: a chronic macrocellular "desquamative" pneumonia. The cells of the alveolar infiltrate showed vacuolization

and decay. We assume that the primary infection and the lymphonodogenic bronchial lesions, producing the perforative scar of the left upper lobe and the calcified focus of the middle lobe, occurred in childhood. The perforative bronchial lesion following lymphonodogenic exacerbation was 2½ to 3½ months old.

A radiograph was taken 17 days before death: aspect of the lesions showed massive subapical condensation of the left upper lobe.

Remarks: The pulmonary infiltration was considered clinically to be a chronic pneumonia caused probably by a virus infection.

Epicrisis: Typical subapical "early infiltration", indicating the initial stage of an exacerbated chronic pulmonary tuberculosis, is the prominent feature of this case. The reactivation of the lymph-node tuberculosis was enhanced by emaciation due to the multiple sclerosis.

Case No. 6. A 22-year-old woman died of pulmonary and enteral tuberculosis, severe anemia and vein thromboses. The autopsy (No. 829/47, Istanbul) disclosed the fresh reactivation of a chronic pulmonary tuberculosis. We observed the moderate enlargement and caseous tuberculosis of lymph nodes of the right intertracheo-broncho-pulmonary spaces, of the right interlobar spaces, and of the bifurcation space. No doubt, the size of the lymph nodes resulted from the diminution of complexes which in early stages of the disease were much larger. Multiple, small, very hard calcium foci were present in lymph nodes of the right hilum and within the pulmonary tissue bilaterally. An extensive, deep perforative defect of the ant. wall of the right main bronchus led into an approximately cherry-sized parabronchial lymph-node cavity; this lesion was accompanied by diffuse caseous bronchitis, and by diffuse dilation of the large and middle-sized bronchi of the middle lobe. Another perforative defect, surrounded by caseous bronchitis, affected the upper lobe main bronchus. The right middle lobe was involved by a massive, homogeneous lobar condensation of rubber-eraser-like consistency; a similar type of segmental pneumonic infiltration, containing caseous areas, affected the right upper lobe. Caseofibrinous pleuritis was present between middle and lower lobes. Microscopic examination of the middle lobe showed: (1) dissolving, predominantly intra-alveolar, macrocellular infiltration (fatty degeneration of alveolar cells; pycnotic processes); (2) few tubercles, mostly in disintegration; (3) sparse, small necroses; (4) beginning perivascular fibrosis, indicating the stage of consolidation of an allergic lymphonodobronchogenic aspiration-infiltration. The upper-lobe condensation displayed, in principle, similar changes; however, necroses (caseous pneumonia) were more emphasized. Tubercles of the infiltrated pulmonary areas contained mostly very few germs (2-30); even necroses within tubercles included only very sparse bacilli. Similarly, very few germs (1-15) were found in areas of desquamative pneumonia. Caseous pneumonic areas contained in general 1-20 agents, and up to 100 germs in a few microscopic fields. The tubercular infection was assumed to have been present since childhood. We believe that the discharge of tuberculous lymph nodes into the bronchi, which introduced the fatal relapse, occurred 2½ to 3½ months before death.

Radiographs taken 60 and 5 days before death revealed infiltration (typical Assmann focus) of right upper lobe, visible in both radiographs; extensive middle-lobe changes, resembling "epituberculous" condensations, also were present in both radiographs. The second radiograph exhibited a disintegrating (cavity?) lymph-node structure at the level of the middle-lobe bronchus.

Remarks: Radiographs disclosed the presence of (spont.) pneumo-thorax at the right side, caused by discharge of softened caseous lymph nodes of the inf. lateral interlobar space simultaneously into the bronchial system and into the pleural cavity.

Epicrisis: Two subapical "early infiltrates", one in subclavicular location (Assman's infiltrate), the other affecting the middle lobe, both condensations being lymphonodogenic aspiration-infiltrations. The lymph-node perforations probably occurred simultaneously. The lobar extension of the middle-lobe involvement apparently corresponded to the fact that the perforative lesion of the middle-lobe bronchus was very large. In spite of the extensive caseous

bronchitis, the number of histologically detectable tubercular bacilli was very reduced, indicating a strong immunity effect.

Case No. 7. An eight-year-old boy died of hepatitis, accompanied by icterus and uremia. The autopsy (No. 497/47, Istanbul) disclosed a tubercular primary infection affecting mainly the right lung. We observed moderate enlargement and caseous tuberculosis of the lymph nodes of the right intertracheo-bronchopulmonary space, of the sup. and inf. lateral and mediodorsal interlobar spaces on the right side, and of the bifurcation space. No doubt, the size of the lymph nodes resulted from the diminution of originally much larger complexes. The interbronchial lymph nodes of the left lung were not involved! The caseated lymph nodes displayed a concentrically stratified structure. Microscopic examination showed that the lymph nodes were calcium-impregnated. Some lymph nodes contained fresh tuberculous granulation. A small lymphonodogenic perforative defect of the stem of the middle-lobe main bronchus was present, covered by polyp-like tubercular granulation tissue; diffuse and sacciform dilation characterized the bronchi of the right middle lobe, distally from the perforative lesion. The markedly shrunken middle lobe displayed a diffuse, rubber-eraser-like lobar infiltration. A lentil-sized, rather hard, concentrically stratified, encapsulated, calcium-encrusted primary focus was located in the right lower lobe. Microscopic examination of the condensed right middle lobe disclosed: (1) diffuse alveolar and interstitial inflammation in regression; (2) tubercular conglomeration with Langhans' giant cells; (3) cicatricial fibrosis; (4) aerated pulmonary parts; (5) absence of necroses, signifying progressive healing of an allergic pulmonary infiltration induced by lymphonodo-bronchogenic superinfection. In a microscopic field of the necrotic area of the primary focus, 160 germs were seen; 10 germs per microscopic field of the fibrous zone surrounding the necrosis. Tubercles of the middle-lobe condensation contained 2-10 germs included in epithelioid cells, 1-2 bacilli being located between these elements. In individual Langhans' giant cells, 1-5 germs were observed. Histological sections of chronic pneumonic areas displayed very few bacilli, located in alveolar cells. We believe that the tubercular infection occurred 6-8 months, and that the lymphonodogenic aspiration began 4 to 6 months before death.

No radiograph was available.

Remarks: The very low number of tubercle bacilli, located in the condensed pulmonary territory, signifies the effect of immunity, which, probably, was in decline, permitting the development of new tubercles in lymph nodes and the proliferation of germs in the primary focus.

Epicrisis: This is a case of healing lobar rubber-eraser-like aspiration-infiltration, following lymph-node discharge in the early stage of a primary infection. Hypersensitivity caused the lobar extension; strong postinfectious immunity explains the predominantly cellular composition of the pulmonary condensation.

Case No. 8. The autopsy (No. 320/48, Istanbul) of a six-month-old girl disclosed tuberculous meningitis, pulmonary and intestinal tuberculosis, caseous tuberculosis of the Fallopian tubes bilaterally, and miliary dissemination following primary infection. We observed intense enlargement and caseous tuberculosis of paratracheal lymph nodes bilaterally; lymph nodes of the interlobar spaces and of the hilum angles bilaterally were also involved. The bifurcation lymph nodes formed a complex larger than two walnuts. The subclavian lymph nodes of the right side were not much smaller! A cherry-sized, empty lymph-node cavity, displaying smooth and rather clean walls at the level of the lateral interlobar space of the left lung, broadly communicated with the proximal part of the main bronchus of the left lower lobe and with the proximal sector of the lingular bronchus. The left lower lobe and the lingular segment of the left upper lobe were considerably enlarged by a diffuse, massive, meaty (rubber-eraser-like), homogeneous infiltration. The axillary segment of the left lower lobe contained an almost prune-sized cavity. Between this cavity and the rubber-eraser-like pneumonic condensation, no particular zone of demarcation was present. Microscopic examination of the pulmonary infiltration revealed a predominantly intra-alveolar accumulation of alveolar histiocytes; scattered epithelioid cell tubercles; a few necroses

in tubercles and in diffusely infiltrated pulmonary parts; bronchi filled with polymorphonuclear leucocytes, i.e., changes signifying an early consolidation stage of an allergic desquamative pneumonia. The tubercular infection occurred 2-3 months before death. We assume that the development of the lymphonodogenic aspiration-infiltrations began 6 to 8 weeks before death.

Remarks: No primary focus could be detected. We assume that it was located in the axillary sector of the left lower lobe and eliminated by the disintegration of the surrounding infiltrated pulmonary tissue.

Epicrisis: The discharge of disintegrated caseous lymph nodes into the main bronchus of the left lower lobe and into the lingular bronchus caused the development of extensive, predominantly macrocellular aspiration-infiltrations. The dissolution of a large part of the desquamative pneumonia occurred shortly before death.

Case No. 9 (Figs. 2 and 9) A 1½-year-old male died of laryngeal and tracheal diphtheria. The autopsy (No. 739/47, Istanbul) disclosed the presence of a tubercular primary infection affecting the left lung. Up to cherry-sized complexes of caseated lymph nodes flanked the trachea bilaterally; a plum-sized caseated lymph-node conglomeration filled the bifurcation space; bean-sized, diffusely caseated interbronchial lymph nodes were located between the main bronchus of the left upper lobe and the—united—axillopectoral and lingular system of the left upper lobe; and an almost plum-sized caseated lymph-node conglomeration distended the lateral interlobar space. Parabronchial lymph nodes of the right lung were intensely involved! A lymphonodogenic perforative defect of the lateral wall of the left lower lobe main bronchus, located at the level of the orifice of the superior dorsal bronchus, just above the orifice of the axillary bronchus, led into a bean-sized, perfectly cleansed lymph-node cavity situated in the lateral interlobar space of the left lung and surrounded by massively caseated lymph nodes. Another perforative lesion involving the proximal sector of the lingular bronchus also communicated with the lymph-node cavity mentioned above. A diffuse, massive, homogeneous rubber-eraser-like infiltration permeated the entire left lower lobe, surrounding an almost plum-sized cavity of the axillary sector. The lingula contained a cherry-sized, roundish cavity, a dissolved aspiration-infiltration. The walls of both cavities were smooth and soft, showing no particular demarcation. Microscopic examination revealed filling of the alveoli and acini with large round cells ("alveolar histiocytes"), i.e., the stage of consolidation of an allergic, lymphonodo-bronchogenic, aspiration-infiltration. Between areas displaying this type of chronic pneumonia, rather fresh necroses were interspersed, indicating the decay of macrocellular pneumonic infiltrates. Necroses of the pulmonary consolidation contained very few germs—only 1-4 in an average microscopic field; chronic pneumonic areas, too, often included only 1-2 bacilli in one microscopic field, mostly in intracellular location. Not one germ was found in nine investigated giant cells of Langhans' type! We assume that the tubercular infection occurred 4-5 months before death and that the development of the lymphonodogenic aspiration-infiltration began 2 to 2½ months before death.

No clinical radiography was available.

Remarks: No primary focus could be detected in this case. We believe that it was destroyed by the disintegration of one of the aspiration-infiltrations. We assume that the cavitation of the aspiration-infiltrations occurred shortly before death.

Epicrisis: Typical instance of chronic, allergic, macrocellular pneumonia, caused by discharge of caseated lymph nodes into the bronchial system. The very low number of tubercle bacilli, observed in the infiltrated pulmonary areas, indicates a strongly effective immunity.

Case No. 10. A five-month-old boy died of pulmonary tuberculosis. The autopsy (No. 617/45, Istanbul) showed moderate enlargement and tuberculous infiltration of the paratracheal lymph nodes, bilaterally; lymph-node tuberculosis of the bifurcation space, of the left lateral and mediodorsal interlobar spaces and of the left hilum angles. The interlobar and peribronchial lymph nodes of the right lung were also involved. A large perforative defect of the anterior wall of the left lower lobe main bronchus was present, at the

level of the medianus orifice, directly below the orifice of the superior dorsal bronchus. This defect was connected with a cherry-sized lymph-node cavity located in the inferior hilum angle (in its lowest sector!). The walls of the lymph-node cavity displayed many tears. A massive lobar condensation ("aspiration-infiltration") of rubber-eraser-like consistency involved the entire (considerably enlarged) left lower lobe containing a walnut-sized cavity of the sector aerated by the descending branch of the superior dorsal bronchus, and a somewhat smaller cavity, located in the sector supplied by the paracardiac branch of the median bronchus. These two cavities were divided by a large area of massive infiltration. No zones of demarcation were present between the cavities and the pulmonary infiltration. Microscopic examination disclosed the stage of consolidation of an allergic chronic pneumonia, caused by superinfection: predominantly macrocellular infiltrate filling acini and alveoli; sparse, relatively small necrotic areas; no tubercular formation; beginning decay of individual cells of the infiltrate. Necroses—even relatively large foci—often contained absolutely no germs, or only 1-2 exemples. In areas of cellular infiltration, most microscopic fields showed no germs; in some areas, single—intracellularly located—bacilli could be detected after thorough search. We assume that the tubercular infection occurred 3-4 months before death. The development of the lymphonodogenic aspiration-infiltration began 1½ to 2½ months before death.

No clinical radiography was available.

Remarks: No primary focus was found; we suppose that it was located in the paracardial sector of the left lower lobe and was destroyed by the disintegration of the surrounding pulmonary infiltrate. We assume that the cavitation developed shortly before death.

Epicrisis: Typical, chronic, macrocellular pneumonia, caused by the discharge of caseous lymph-node masses into the bronchial system. There was a very low number of tubercle bacilli, indicating highly effective immunity.

GROUP III.

CASES OF MASSIVE AND CAVITATED, REGRESSIVE CASEOUS-PNEUMONIC INFILTRATIONS

Case No. 1. (Fig. 5 of our paper in Arch. Ped., Vol. 74, 1957, p. 169). The autopsy (No. 598/47, Istanbul) of a two-month-old girl, who died of pulmonary tuberculosis, revealed a massive, wedge-shaped caseous infiltration in a large subapical segment, aerated by the post. oblique bronchus of the left upper lobe, and accompanied by bilateral, macronodular hematogenic dissemination. The paratracheal lymph nodes bilaterally, lymph nodes of the left lateral and mediodorsal interlobar spaces, lymph nodes of the hilum angles left and of the bifurcation spaces, as well as the interlobar and interbronchial lymph nodes of the right lung, were considerably enlarged and affected by caseous tuberculosis. Discharging disintegrated caseous lymph nodes located in the anterior hilum angle of the left lung destroyed the superior and anterior walls of the left main bronchus and of the main bronchus of the left upper lobe, producing a deep and wide parabronchial lymph-node cavity. Microscopic examination of the left upper lobe showed beginning dissolution of extensive necroses; macrocellular, chronic pnuemonic infiltration between necrotic areas, indicating consolidation of an allergic process induced by superinfection; absence of typical tubercular structures, and a few, scattered giant cells of Langhans type, situated intra-alveolarly.

The wall of the lymph-node cavity contained up to 3000 germs in one microscopic field! In an average microscopic field of structureless debris, loosely filling the lymph-node cavity, 255 bacilli were enclosed in histiocytes and 583 germs in necrotic lumps. In lymph nodes surrounding the lymph-node cavity, epithelioid cells of tubercle contained 70-100, necroses 550-770 germs in a microscopic field. In caseous pneumonic areas 1200-1900, and in macrocellular infiltrates 10-500 tubercle bacilli were counted in a microscopic field; many germs were included in polymorphonuclear leucocytes!

No radiography was available.

Remarks: No primary focus was observed; we assume that it was enveloped by the necrotic masses of the aspiration-infiltration. The contamination occurred at birth, by the mother, who died immediately after delivery of pulmonary tuberculosis. This case is particularly valuable because it proves that just as in pre- and super-infected animals, a period of two months suffices to produce a very extensive caseous pulmonary infiltration, consequent to lymph-node discharge in a spontaneous disease.

Epicrisis: Extensive caseous necrosis of a macrocellular, allergic, lymphonodogenic aspiration-infiltration. The high number of tubercle bacilli indicates an initial stage of the process, in which the—undoubtedly present—postinfectious immunity was not able to develop its maximum effect. On the other hand, we also have to consider the occurrence of an inflammatory fixation-phenomenon: four weeks after infection, tubercle bacilli circulating in the blood were attracted into the inflammatory area produced by the lymphonodogenic superinfection.

Case No. 2. Autopsy (No. 821/47, Istanbul) of an eight-month-old boy who died of tuberculous meningitis and pulmonary tuberculosis, revealed a fresh primary infection of the left lung. Up to cherry-sized caseated lymph nodes, often joining to form quite large complexes were located paratracheally on both sides; quite large caseous lymph nodes filled the bifurcation space, the interlobar spaces and the hilum angles bilaterally. Interbronchial lymph nodes of the right lung were up to bean-sized and diffusely caseated. A perforative lesion of the proximal part of the left lower lobe main bronchus, at the level of the orifice of the superior dorsal bronchus and just below the common orifice of the lingular and of the axillopectoral system of the left upper lobe, was caused by the discharge of a softened, disintegrated caseous lymph node of the inferior hilum angle. The most important pulmonary lesions were: (1) A pea-sized, roundish, caseous, primary focus of the axillar sector of the left lower lobe, 1 cm. above the basal border. The primary focus displayed a hint of concentric structure and was surrounded by a grayish infiltrate. (2) A massive, diffuse, caseous condensation of the apical sector of the left lower lobe, aerated by the apical and the horizontal branches of the superior dorsal bronchus; and an adjoining, extensive rubber-eraser-like condensation of the dorso-paravertebral part of the left lower lobe, supplied by the descending branch of the sup. dorsal bronchus. (3) A massive, caseous pneumonic infiltration of the paracardiac sector of the left lower lobe (4) An extensive, massive, caseous pnuemonic infiltration of the lingular and of the axillopectoral sectors of the left lower lobe. (5) Scattered macronodular bronchogenic and diffuse hematogenic spread in both lungs. Microscopic examination revealed: (1) Caseous pneumonia, developed evidently shortly before death by necrosis of macrocellular, chronic-pneumonic condensation. (2) Macrocellular infiltration (early stage of consolidation). (3) Tubercular structures displaying healing tendency. (4) Filling of the bronchi by aspirated detritus. The entire necrotic area of the primary focus contained only 15 germs; in 8 tubercles of the infiltrate surrounding the primary focus, an average of 1-3 germs was found after thorough search, located in epithelioid elements, in necroses or in Langhans' cells. In other 11 tubercles of the perifocal condensation not one germ could be detected! In 56 tubercles of the infiltrated pulmonary tissue, no more than 1-2 germs in each could be found after long examination; 41 other tubercles proved free of germs. In areas of caseous pneumonia, 32 microscopic fields were investigated; in 26, no more than 1-20 germs were observed. Six microscopic fields, however, contained 46, 171, 132, 84, 227 and 218 bacilli each. In macrocellular (rubber-eraser-like) infiltrates, no agents could be observed. We assume that the tubercular infection took place 2-3½ months, and that the discharge of tubercular lymph nodes into the bronchial system, followed by the development of the aspiration-infiltration, occurred 1-1½ months before death.

Radiography, taken one day before death, showed many lymph nodes, particularly on the right side, and extensive pulmonary condensations bilaterally. The primary focus was clearly visible!

Epicrisis: Typical, caseous lymphonodogenic aspiration-infiltration, accom-

panied by extensive rubber-eraser-like pulmonary condensations. The average low—often very low—number of tubercle bacilli indicates the effect of a strong immunity.

Case No. 3. The autopsy (No. 186/47, Istanbul) of a four-month-old boy disclosed a primary tubercular infection of the left lung. The paratracheal and interlobar, interbronchial and bifurcation lymph nodes, as well as the lymph nodes of the hilum angles, although of moderate size, were thoroughly caseated; we had the impression that they diminished in volume after a previous stage of considerable swelling. A narrow perforative defect of the proximal part of the left lower lobe bronchus was caused by the discharge of softened, disintegrated, and cavitated caseous lymph nodes of the left interlobar space. We observed: (1) a cherry-stone-sized, concentrically stratified, round primary focus, located in the lingular tip, surrounded by a small zone of (perifocal") infiltrate; (2) a massive, extensive, diffuse, predominantly caseous infiltration of the inferior two-thirds of the left lower lobe, displaying areas of beginning disintegration; (3) cherry-sized, massive caseous condensation of the central basal sector of the right lower lobe; (4) macronodular hematogenic dissemination in both lungs. Microscopic examination revealed predominantly caseous pneumonic infiltration in disintegration. The spaces between necroses displayed a typical macrocellular, allergic, chronic pneumonic condensation in the stage of beginning consolidation; numerous Langhans' cells, intra-alveolarly located; many polymorphonuclear leucocytes and very few tubercular structures. Areas of caseous pneumonia contained 10-80 germs in one microscopic field; areas of macrocellular infiltration: mostly no more than 2-3 (intracellularly located) agents in one microscopic field; exceptionally 8-10 bacilli. Tubercular structures included only 2-7 germs in one tubercle, Langhans' giant cells, never more than 1-2 agents. We assume that the child was infected three months, while the bronchial perforation occurred 1½-2 months before death.

No clinical radiography was available.

Epicrisis: This is the case of a typical lymphonodogenic aspiration-infiltration. The very low number of tubercle bacilli indicates the influence of a highly effective immunity.

Case No. 4. The autopsy (No. 701/47, Istanbul) of a 17-year-old male revealed tuberculous meningitis, probably the consequence of a post-primary lymphonodogenic relapse. Plum-sized caseous lymph nodes of the left lung, forming up to goose-egg-sized conglomerations in the bifurcation space and in the lateral interlobar space predominated. A walnut-sized caseated lymph node of the lateral interlobar space was transformed into a lymph-node cavity. Large, caseous lymph nodes flanked the trachea on both sides. The lymph nodes of the mediodorsal interlobar space and of the hilum angles of the left lung were considerably swollen and thoroughly caseated. The lymph nodes of the right lung also were involved. A very large perforative defect of the stem of the lingular bronchus of the left lateral interlobar space produced the discharge of softened and disintegrated masses. The lingular segment of the left upper lobe was intensely enlarged, giving the impression of an independent lobe, affected by lobar pneumonia: a diffuse, massive infiltration, characterized primarily by a condensation of rubber-eraser-like consistency, with quite extensive caseous areas. Particularly interesting were very numerous, markedly dilated bronchi filled with aspirated caseous masses. A rather fine-nodular miliary dissemination was present bilaterally. Microscopic examination disclosed lobular caseous pneumonic areas, in which the shadows of the original pulmonary structures (bronchi, alveolar septa and of the intra-alveolar macrocellular infiltrate) remained clearly recognizable. The rubber-eraser-like areas showed the typical aspect of an allergic, chronic desquamative pneumonia in consolidation. A few Langhans' cells were located intra-alveolarly. The average number of tubercle bacilli was minimal in both caseous and macrocellularly infiltrated areas: 3-12 in a microscopic field. In many microscopic fields only 1 or 2 germs were detected after long and thorough search. On the other hand, however, a few microscopic fields of caseous pneumonic areas contained up to 500 germs! Miliary tubercles were almost free of bacilli. We assume that the tubercular infection probably existed since childhood, and that the discharge of caseated lymph nodes producing the pulmonary infiltration occurred 4-5 months before death.

Radiographs were taken 3½ months, 2¾ months, 2 months and 9 days before death. The first radiograph already disclosed an extensive lingular condensation, large lymph nodes of the lateral interlobar space of the left lung and considerably enlarged lymph nodes of the right hilum. The later radiographs were complicated by an artificial pneumothorax on the left side.

Remarks: No primary focus was found. Considering the age of the patient, we are inclined to assume that, in this case, we deal with consequences of exacerbation of a lymph-node disease latently present since childhood.

Epicrisis: Typical, extensive aspiration-infiltration of lymphonodogenic origin, the appearance of which, thanks to a radiograph, could be dated quite exactly. Powerful immunity reduced the number of tubercle bacilli to a minimum in most areas of the condensation.

Case No. 5. (Fig. 10) The autopsy (No. 885/47, Istanbul) of a six-year-old boy disclosed tuberculous meningitis and peritoneal tuberculosis, consequent to a primary infection of the right lung. Up to cherry-sized swollen and diffusely caseated lymph nodes surrounded the trachea and filled the bifurcation space, the interlobar spaces of the right lung, as well as the hilum angles. Smaller caseated lymph nodes were present in the interbronchial angles of the right upper lobe. A cherry-sized parabronchial lymph-node cavity was produced by the discharge of caseous lymph nodes of the anterior hilum angle into the common stem of the axillopectoral system of the right upper lobe. This lymph-node cavity was filled with mastic-like, rather dry, necrotic masses; after their elimination a large bronchial defect became visible, completely severing the stem of the axillopectoral system from its branches. A smaller perforative lesion of the right stem bronchus was caused by the discharge of a lymph node of the inferior hilum angle. Further tubercular lesions were the following: (1) A lentil-sized, hard, primary focus of the right lower lobe, in advanced cicatrization; (2) extensive, massive, diffuse caseous pneumonia, affecting the entire axillopectoral segment of the right upper lobe. The necrotic masses were dry, mastic-like, displaying clear lobular arrangement, the individual caseous fields being separated from each other by bands of grayish-pink connective tissue. Microscopic examination of the pulmonary infiltration revealed an advanced healing process, characterized (1) by cicatricial demarcation of the necrotic areas; hyalinization and splitting of tubercles; diffuse fibrotic devastation of pulmonary tissue; (2) by cleansing and reaerating of infiltrated pulmonary areas. Many bronchi were filled with aspirated necrotic masses. We believe that the tubercular infection occurred 9-12 months before death. Thus, the perforative bronchial lesion, which caused the pulmonary infiltration, was approximately 8-10 months old.

Radiograph taken 17 days before death displayed shadows of large lymph nodes of the right hilum, surrounded by pulmonary condensation.

Remarks: We assume that an exacerbation of the lymph-node tuberculosis occurred shortly before death, inducing meningitis.

Epicrisis: The extensive aspiration-infiltration in this case displayed advanced healing tendency, clearly demonstrating that even extensive necroses cannot be considered unconditionally as indicating unfavorable involvements.

Case No. 6 (Figs. 11 and 12) The autopsy (No. 32/48, Istanbul) of a three-year-old girl revealed very large caseated lymph nodes of the right intertracheo-bronchopulmonary space (goose-egg-sized conglomerate!), of the bifurcation space (walnut-sized cavitated complex!), and of the interlobar spaces and of the hilum angles. These lymph nodes seemed to have surpassed their maximum enlargement, and, because of disintegrative processes, they began to become deflated. The lymph nodes of the left side were small, and, even if involved, displayed only minor changes. Multiple perforative bronchial lesions affected the right lung: We observed (1) a perforative defect of the medial wall of the right stem bronchus, communicating with a walnut-sized lymph-node cavity of the right-sided bifurcation lymph-nodes; (2) a lentil-sized perforative defect of the main bronchus of the middle lobe near to its orifice, connected with a cherry-sized lymph-node cavity of the inferior hilum angle; and (3) mutilation of the stem of the median bronchus of the lower lobe by the same lymph node which discharged into the middle-lobe bronchus. The following involvements of the pulmonary tissue were present:

(1) a lentil-sized, irregularly wedge-shaped, caseous primary focus of the right lower lobe, located dorsally, 2 cm. above the basal border; (2) a dense, caseous and rubber-eraser-like pneumonic infiltration of the right middle lobe and of the right lower lobe; (3) a large cavity of the right lower lobe, affecting the paracardial sector, supplied by the median bronchus; (4) a rather dense, micronodular, hematogenic miliary dissemination in both lungs. Microscopic examination showed: (1) caseous pneumonic areas in which the necrotic process was still expanding: the lobuli were characterized by large central necroses advancing in the direction of the lobular septa; (2) an intra-alveolar cellular infiltration displaying alveolar histiocytes, polymorphonuclear leucocytes, lymphocytes and Langhans' cells, intra-alveolarly located; (3) filling of the bronchi with aspirated necrotic detritus; (4) rather extensive atelectatic collapse. Practically no tubercular structures were present! In this case, the number of tubercle bacilli detected in histological sections was relatively high in all types of pulmonary changes. In areas of caseous pneumonia, up to 1500-2500 germs were seen in one microscopic field. The bacilli were often located in shadows of necrotic alveolar cells! In areas of cellular infiltration, up to 500 germs existed in one microscopic field. We assume that the tubercular infection occurred 2½-3 months, and the lymphonodogenic bronchial lesions 5-7 weeks before death.

Radiograph taken three days before death displayed: (1) large lymph nodes of the right intertracheo-bronchopulmonary space; (2) large lymph nodes of the sup. and inf. lateral interlobar spaces of the right lung; (3) a large cavity of the paracardial segment of the right lower lobe.

It seems that the cavity of the right lower lobe developed shortly before death.

Epicrisis: Multiple, extensive aspiration-infiltrations corresponding to multiple, large lymphonodogenic bronchial lesions are present in this case. The high number of tubercle bacilli indicates the initial stage of the allergic condensation in which immunity has not destroyed the agents as yet, although probably being capable of inhibiting their growth and counterbalancing their inflammatory influence. Also, we have to consider the effect of an inflammatory fixation-phenomenon. (See Case I of this Group.)

Case No. 7 (Figs. 13 and 14) The autopsy (No. 3/48, Istanbul) of a 1½-year-old girl, who died of tuberculous meningitis, disclosed a primary infection affecting the right lung. Large, caseous paratracheal lymph nodes on the right side formed massive complexes; voluminous, caseous lymph-node conglomerations filled the bifurcation space, the interlobar spaces and the hilum angles of the right lung. Lymph nodes of the left lung were not involved. Moreover, we observed (1) the mutilation of the main bronchus of the right upper lobe, subsequent to the discharge of caseous lymph nodes of the ant. hilum angle; (2) a perforative defect of the lateral wall of the right stem bronchus, caused by the discharge of a lymph node of the sup. lateral interlobar space. This perforative lesion led into an almost cherry-sized lymph-node cavity, connected with a large parenchymal cavity of the upper lobe. The following pulmonary lesions were present: (1) a giant cavity of the right upper lobe, produced by the disintegration and elimination of a lobar aspiration-infiltration; (2) filling of the entire right middle lobe and entire right lower lobe with a massive, diffuse, partially rubber-eraser-like, partially caseated aspiration-infiltration; (3) macronodular hematogenic dissemination of the left lung. Microscopic examination showed: (1) caseous pneumonic areas: typical changes indicating that the process surpassed its acme; (2) chronic pneumonic condensations: macrocellular intra-alveolar accumulations (stage of consolidation), the alveolar histiocytes containing mostly fat droplets; Langhans' giant cells located intra-alveolarly; (3) sparse tubercular structures. (4) bronchi of the infiltrated areas were filled with detritus. As to the presence of tubercle bacilli in histologic slides: (1) In areas of caseous pneumonia: Germs could be found only after long and thorough search; no more than 1-2 in each microscopic field. (2) In tubercles: In necroses, as well as in epithelioid cells, mostly very few germs were present. The lowest number of observed bacilli was 5, the highest 75 in one tubercle.

We estimate that the tubercular infection occurred 3-4 months, the lymphonodogenic bronchial lesions 2-3 months before death.

Radiograph taken five days before death showed: (1) the large cavity of the right upper lobe; (2) massive condensations of middle and lower lobes; (3) numerous enlarged lymph nodes of the right lung, and, (4) hematogenic dissemination in the left lung.

Remarks: No primary focus was found. We believe it was located in the right upper lobe, being destroyed by the disintegration of the lobar aspiration-infiltration. The cavity of the right upper lobe—its extension, form, and pathogenesis—very much resembles the giant cavity in Fig. 6 of our previous paper, "Exp. basis, etc." in Arch. Ped., Vol. 75, p. 315, 1958.

Epicrisis: Typical multifocal tuberculous pulmonary involvement caused by multiple lymphonodogenic bronchial perforative lesions. The low number of tubercle bacilli indicates the effect of a vigorous immunity. No doubt, the giant cavity does not signify an aggressively progressing process!

EXPLANATION OF THE SIGNS IN THE FIGURES

We employ for the abbreviation of the names of the pulmonary lobes, the tracheobronchial system, the paratracheal and parabronchial lymph nodes, the vessels, and the parapulmonary spaces the following symbols:

A aorta; *P* pulmonary artery; *sc* subclavian artery; *S* upper lobe; *M* middle lobe; *Li* lingula; *I* lower lobe; *BD* right main bronchus; *BS* left main bronchus; *BT* stem bronchus; *b* bronchus in general.

Bronchi of the upper lobes.

sB main bronchus of the upper lobe; *bap* common stem of the axillo-pectoral system; *haa* ant. horizontal axillary bronchus; *hp* pectoral bronchus; *hap* post. horiz. axillary bronchus; *hd* horizontal dorsoparavertebral bronchus; *oa* ant. oblique bronchus; *op* post. oblique bronchus; *va* ant. vertical bronchus; *vp* post. vertical bronchus.

Bronchi of the (right) middle lobe.

mB main bronchus of the middle lobe; *ma* anterior branch; *mp* post. branch.

Bronchi of the lingula.

lB main bronchus of the lingula; *ma* ant. branch; *imp* post. branch.

Bronchi of the lower lobes.

iB main bronchus of the lower lobe; *ds* superior dorsal bronchus of the lower lobe; *dd* descending branch of the sup. dorsal bronchus; *m* median bronchus; *a* axillary bronchus; *ac* paracardial branch of the axillary bronchus; *di* inferior dorsal bronchus; *bl* lateral basal bronchus; *bc* central basal bronchus; *bm* medial basal bronchus.

The parapulmonary spaces.

TBP intertracheo-broncho-pulmonary space; *B* bifurcation space; *Is* superior lateral interlobar space of the right lung; *Ii* inferior lateral interlobar space of the right lung; *Il* lateral interlobar space of the left lung; *Imd* medio-dorsal interlobar space.

Lymph nodes.

Ll lymph nodes in general; *TL* paratracheal lymph nodes; *Ly* paratracheal lymph nodes, located below the right subclavian artery; *sL* lymph nodes of the superior lateral interlobar space of the right lung; *sLs* supra-arterial lymph nodes of the sup. lat. interlobar space of the right lung; *sLi* intra-arterial lymph nodes of the sup. lat. interlobar space of the right lung; *iL* lymph nodes of the inferior lateral interlobar space of the right lung; *lL* lymph nodes of the medio-dorsal interlobar space; *mLs* supra-arterial lymph nodes of the medio-dorsal interlobar spaces; *mLi* infra-arterial lymph nodes of the medio-dorsal interlobar spaces; *BL* bifurcation lymph nodes; *BLd* right bifurcation lymph nodes; *BLs* left bifurcation lymph nodes.

Branches of the pulmonary artery.

The same symbols as for the concurrent bronchi, only in the place of *B* or *b*, *A* or *a*: (for example; main artery of the middle lobe: *mA*; or, axillary artery of the lower lobe: *aa*).

UNDERDEVELOPMENT OF THE LEFT AURICLE AND LEFT VENTRICLE WITH HYPOPLASIA OF THE AORTA

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The exact incidence of this rare lesion has not been estimated owing to the different terms employed. Cases have been reported under the titles of congenital aortic stenosis, congenital aortic atresia, hypoplasia of the left ventricle, congenital mitral atresia, etc. Friedman, Murphy and Ash[1] described three cases of aortic atresia and tabulated forty-one others. They also gathered forty-five cases of combined aortic and mitral atresia from the literature.

CASE REPORT

A three-month-old female, Sinhalese infant, was admitted to the Lady Ridgeway Hospital for Children, Colombo, with a history of fever and difficulty in breathing of one week's duration.

This was the youngest child in a family of three children. The mother did not have hyperemesis, fever or other abnormality during pregnancy and this baby was born normally at term at the De Soysa Maternity Hospital. The birth weight was seven pounds. The parents did not give any history of consanguinity. The other two children were normal and well. The patient did not show any signs of cyanosis or fever before the present illness.

Examination revealed a fairly well-nourished baby, though the weight was only eight pounds and six ounces. The child was severely dyspnoeic, with tachycardia and central cyanosis but no clubbing of the fingers and toes. On examination of the heart, no murmurs or abnormal heart sounds were detected. Fine crepitations at the end of inspiration were heard over both sides of the lungs. The liver was palpable two fingers below the costal margin but it was not pulsatile nor tender. The spleen was not palpable. There was no oedema of the lower limbs. The child expired within forty-five minutes of admission.

At autopsy there was consolidation of the upper third of the right lower lobe and of the lower third of the right upper lobe. There was also consolidation of the anterior and upper parts of the

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left lower lobe of the lung. On histological examination the endocardium did not show any evidence of endocarditis but the lungs showed evidence of bronchopneumonia.

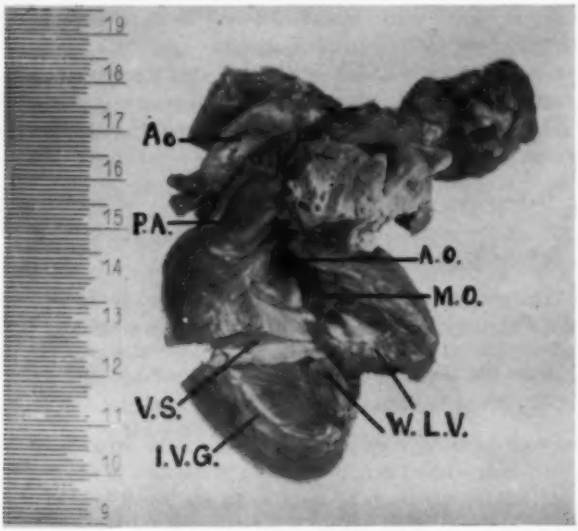

Fig. 1. Small aorta (Ao), large pulmonary-artery (P.A.), and thick interventricular septum (V.S.) with wedge sections removed. The anterior descending branch of the left coronary artery (L.C.A.) is seen in the interventricular groove (I.V.G.). The endocardial surface of the left ventricular cavity (W.L.V.) shows the well formed papillary muscles. The aortic orifice (A.O.) and the mitral orifice (M.O.) are also seen.

The pericardium was normal but the heart was enlarged. There was gross enlargement of the right ventricle with enlargement of the right auricle and pulmonary artery. The superior and inferior venae cavae drained into the right auricle. The pulmonary veins entered the left auricle. Both this chamber and the left ventricle were unduly small. There was a gross defect in the inter-auricular septum whereas the interventricular septum was well formed and very thick, even thicker than the hypertrophied right ventricular wall. The aorta arose from the left ventricle and was narrower than normal. Its diameter was about two-thirds that of the pulmonary artery.

The mitral and aortic valves were well formed although there was slight narrowing of the mitral orifice only. The tricuspid and pulmonary orifices were normal. The ductus arteriosus was patent but narrow. (Fig. I)

DISCUSSION

In congenital hypoplasia of the left heart there is underdevelopment of the left atrium and the left ventricle. The left ventricle may be very small with a cavity of only 1 or 2 cm. in length lying to the left of the interventricular septum.

Friedman, Murphy and Ash[1] believed that there was always an obstructing deformity, whether atresia or severe stenosis at the aortic or mitral orifice or at both. They therefore recognised three pathological groups viz.

1. Hypoplasia of the left heart with atresia or severe stenosis of the aortic valve. Here the mitral valve was diminutive but otherwise normally formed.

2. The mitral valve was atresic or showed severe stenosis, while the aortic valve was normally formed but small.

3. Both the aortic and mitral valves showed atresia or severe stenosis. Of these, group (1) was the rarest.

Our case however does not fit into any of the above groups and the main obstruction (if at all present) to the flow of blood through the left side of the heart appears to be the small size of the left ventricle.

A patent foramen ovale as in this case, or vascular connections between the left atrium and the left innominate vein or superior vena cava (McIntosh[3], and Edwards and Du Shane[4],) or anomalous pulmonary veins entering the right atrium (Scribe[5],) are usually present. The ductus arteriosus is patent in mitral and aortic atresia or severe stenosis (Friedman et al.[1])

There is no ventricular septal defect in a case of atresia or severe stenosis of both aortic and mitral valves, although a high ventricular septal defect is usually present in cases of pure mitral valve atresia.

In our case the pathway of blood flow was probably as follows: venous blood from the inferior and superior venae cavae entered the hypertrophied right atrium and thence through the tricuspid orifice into the hypertrophied right ventricle. From here it went to the lungs via the pulmonary artery. The blood from the lungs entered the small left atrium via the pulmonary veins and meeting the resistance of a small left ventricle was mainly shunted through the large patent foramen ovale to the right atrium.

Part of the blood from the left atrium however probably entered

the left ventricle and then the aorta. Some of the mixed venous and arterial blood from the pulmonary artery would have entered the aorta through the patent ductus arteriosus as happens in the fetal circulation.

The absence of cyanosis until the present illness viz. pneumonia, was probably due to most of the blood in the aorta being oxygenated. In our case the cyanosis may have been not only due to the pneumonia but also due to increased peripheral pulmonary resistance in the lungs (due to pneumonic consolidation) and to a consequent reversal of this shunt of blood at the foramen ovale i.e. from the right atrium to the left atrium. Friedman et al[1], noted that there is a possibility of a closure of the patent ductus even in the presence of an adequate atrial septal defect. They thought that such a closure of the patent ductus or of the foramen ovale may account for the sudden dyspnoea, cyanosis and heart failure, after a brief benign course. In our case the patent ductus arteriosus may have been wider before death. However, the presence of anoxia and increased pulmonary arterial tension terminally would have opposed closure of the ductus arteriosus. (Nadas[6]).

EMBRYOLOGY

The right and left ventricles are formed during intrauterine life by two excavations which arise in the common ventricle and extend downwards on each side. The intermediate portion of the floor of the ventricular cavity persists as the muscular interventricular septum. (Fraser, J. E.[5])

The two ends of the growing crescentic plate (interventricular septum) join the dorsal and ventral endocardial cushions at about the fifth week of intrauterine life. This septum has a gap which permits the right and left ventricles to communicate and this is called the interventricular foramen. By the end of the seventh week tissue from the structures surrounding the foramen viz. the proximal bulbar septum and the fused middle portions of the endocardial cushions, together with the ventricular septum proliferates and closes the foramen. This is now called the septum membranaceum while the original septum becomes the septum musculare. (Arey, L. B.[7])

Monckeberg (cited by Friedman et al,[1]) believed that congenital aortic stenosis or atresia resulted from an abnormal deviation of the spiral septum which divides the common truncus arteriosus

into the aorta and pulmonary artery during the period when torsion of the bulbus cordis occurs.

The small left auricle and small left ventricle may have been due to the "shift to the left" of the atrio-ventricular septum. (Monckeberg, cited by Large[9]). Atresia of the mitral valve is not necessarily present; only stenosis may exist when the atrioventricular septum is shifted to the left, (Large[9]).

The right auricle and ventricle maintained the systemic circulation through the patent ductus arteriosus and foramen ovale therefore leading to hypertrophy and dilatation of these chambers, (Lippincott.[10])

However, if the auriculo-ventricular septum were shifted to the left, the auriculo-ventricular groove should also be similarly shifted. But in our case, on the external surface of the anterior cardiac face, the anterior interventricular groove lay very much to the right of the thick interventricular septum suggesting that the apportioned portion of the left ventricle has not been excavated up to this boundary.

In the atrial region the incomplete interatrial septum was situated just to the left of the superior and inferior venae cavae, showing that the relation of these orifices to the septum was normal and therefore no shifting of the interatrial septum had occurred. The left atrium was small and the smooth part of the left atrium was visibly constricted at the site leading to the embryological left atrium (auricle) and the auricle itself was small.

The primary abnormality in our case therefore does not seem to be an obstructing deformity at the aortic or pulmonary orifices nor a "shift to the left" of the interatrial and interventricular septa but one of primary failure in development of the left half of the heart although the above mentioned embryonic units persist. The cause of the failure seems to be obscure. The deviation of the spiral septum is not significant as the aortic stenosis was slight and the aortic and pulmonary valves normal.

SUMMARY

1. A case of congenital heart disease with underdevelopment of the left auricle and left ventricle with hypoplasia of the aorta is described.

2. It is suggested that it has been due to primary underdevelopment of the left side of the heart and not due to an obstruc-

tive lesion or "shift to the left" of the auriculo-ventricular septum.

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SEBORRHEA CAPITIS

Clinical Effectiveness of a New Therapeutic Agent

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The seborrheic diathesis is a dysfunction of the sebaceous glands which may occur wherever sebum is secreted and in every age group[1]. Among the diseases resulting from this dysfunction are acne, ceruminosis, seborrheic dermatitis and pityriases simplex and steatoides. In the infant, one of the most commonly encountered seborrheic dysfunctions is "cradle cap," or seborrhea capitis.

Seborrhea capitis is often associated with a mixed infection of Pitysporum ovale (a lipophilic fungus), micrococci, and staphylococci nurtured on the seborrheic substrate provided by hyperactive sebaceous glands.[2] This infection may cause a hyperplasia of the outermost layer of cells in the stratum corneum, resulting in hyperkeratosis with scale and crust formation. Histological examination of these scales usually reveals evidence of the bacterial invasion, and the epithelium, appropriately sectioned and stained, demonstrates the presence of Pitysporum ovale.[3]

This infectious-seborrheic substrate, as a result of its high protein and lipid contents, offers optimum conditions for the development and growth of these invading organisms. Once they have established a foothold in the substrate, the rete mucosum reacts with tissue edema and there is an inflammatory infiltration of the epithelium, a hypertrophy of the deep layer of stratified squamous epithelium and local leukocytosis in the midcorium.

The fatty scales and crusts that form in this condition often mat the hair to the scalp. In the "dry" type of seborrheic capitis the scales are small and easy to remove, but in more serious cases the matted encrustations, by traumatizing the hair follicles, can give rise to either temporary or permanent alopecia. Perifollicular erythematous macules develop and, in time, become confluent; when aggravated they develop into an acute, weeping eczematous dermatosis.

Seborrhea capitis in infants (cradle cap) presents a three-pronged challenge of etiology, basic therapy, and symptomatic relief. Symptomatic relief is often the most important factor involved in bringing immediate comfort to the child and improving a bad cosmetic situation. The basic therapy should, of course, be directed to the underlying etiologic factors, but, too often, treat-

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ment of the seborrheic state is a time-consuming and uncertain procedure.[2]

Effective removal of the scales and crusts of seborrhea capitis and cleansing of the seborrheic substrate is the most adequate type of symptomatic therapy of 'cradle cap." Once these are removed, the scalp, if maintained in a hyposeborrheic state, will resist further infection while the underlying seborrheic diathesis can be attacked.

This cleansing of the scalp can best be effected by an agent which is directly aimed at emulsifying and dispersing the complex lipids in sebum as well as disorganizing the protein component of the crusts and scales. A drug for this condition should also contain a specific antibiotic for the bacteria and fungi involved in the seborrheal infection. The vehicle employed should be aqueous-miscible so that the seborrheic exudate, once emulsified and dispersed, can be easily rinsed off with water. The pH of the preparation should be acid to maintain the natural pH of healthy skin. Since those patients with a basic seborrheal diathesis are prone to contact dermatitis, the agent should have a very low sensitization and irritation potential. Promising reports of a new preparation, Soropon, Pediatric,* aimed specifically at correcting seborrhea capitis led to a study of this agent's efficacy.

MATERIAL AND METHOD

The test preparation* used in this study consisted of a triethanolamine polypeptide cocoate in a vehicle of propylene glycol with tyrothrycin, and Parabens® as a preservative agent. The detergent and emulsifying actions of this preparation are designed to disorganize the protein and fatty components of the crusts and scales of seborrhea capitis. The aqueous miscibility of propylene glycol allows the softened and disintegrated crusts to be rinsed easily from the scalp; the antibacterial agent is then brought into direct contact with the organisms responsible for the infectious phase of the seborrheic dermatitis.

Our study included 48 patients, all with varying degrees of seborrhea capitis. Forty-seven were infants between the ages of 3 weeks and 2 years, while one was a sixteen year old girl. This latter patient was of particular interest since she was a hypothyroid with a lifelong history of dry seborrhea capitis.

* Soropon Pediatric, supplied by the Medical Department of The Purdue Frederick Company, New York, N. Y.

Many of these children presented concomitant skin diseases such as facial eczema, intertrigo, and "diaper rash," pointing to a generalized seborrheic state. Most of these children had been treated unsuccessfully with other dermatological preparations (Table I).

The method of treatment consisted of rinsing the scalp with warm water, then applying 3 to 5 cc. of the test antiseborrheic. A small pad of soft flannel was used to massage the scalp gently but vigorously. Caution was taken not to traumatize the skin. The preparation was allowed to remain in contact with the scalp from 5 to 10 minutes. After this, the scalp was rinsed with warm water and rubbed gently with soft flannel to remove the softened scales and crusts. The scales and crusts were usually loose enough to be removed by simple rinsing; when necessary, however, they were carefully rubbed off using the test solution as a vehicle. When a single application was not sufficient to remove all the material, the treatment was repeated at once.

Eight typical cases in which the test agent was effective — Table I

Case	Age	Sex	Scalp area involved	Concomitant diseases	Comments
1	15 mos.	M	entire	facial eczema	Eczema cleared once seborrheal condition was controlled
2	7 mos.	F	3/4	ceruminosis body eczema	Soropon cleared eczematous scales of body with excellent results, remission of symptoms
3	3 mos.	M	1/2	urticaria diaper rash intertrigo	No allergenic reactions on repeated use, despite history of patient sensitivity to skin irritants
4	1 mo.	F	entire	allergic eczema	Patient received antiallergic diet. Soropon kept scalp clean
5	4 mos.	F	1/4 - 1/2	pyoderma seborrhea dermatitis of face	Scalp clear, facial seborrheal dermatitis improved
6	1 mo.	F	entire	carbuncles and pustules on back of neck and forehead	Antibiotic therapy continued to control skin infections
7	11 mos.	M	entire	eczema of face and arms asthmatic bronchitis	Soropon controlled scalp condition with intermittent maintenance therapy
8	13 mos.	M	1/4 - 1/2	facial eczema	Eczema rescinded as scalp cleared

Associated with the seborrhea capitis there were, in the entire group of 48 cases, 23 patients with eczema, 5 with ceruminosis, 3 with "cradle cap", 2 with intertrigo, 2 with pyoderma, 2 with asthmatic bronchitis, 1 with seborrhea dermatitis, 1 case of thrush and one with carbuncles.

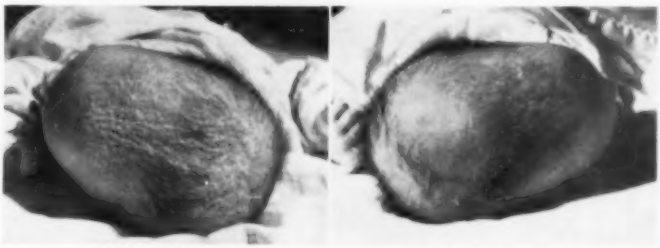
In those cases with a lesser degree of involvement, the procedure was repeated once a week for one month and then as often as necessary. Where the seborrhea capitis was more severe, the above method was used two to three times weekly for one month, once weekly for another month, and then as often as necessary.

RESULTS

Results (Table I and Fig. 1) were evaluated as effective or ineffective. Treatment was considered effective if the encrustations

were easily removed by one or two applications and the scalp kept free of subsequent involvement. Treatment was classed as ineffective when the test agent did not successfully remove the encrustation and exfoliation continued despite continued therapy.

The test agent was effective in all cases. The scales and encrustations in all 47 patients were removed with one to three applications. Where more than one application was necessary, gentle massage was extremely effective in removing the scales. Maintenance therapy was uniformly successful. In the case of the sixteen-year-old, hypothyroid girl, the test antiseborrheic controlled the dry seborrheal exfoliation of the scalp for the first time in the patient's experience.



Before Therapy After Therapy

FIGURE I — Case History

J. D., a 5 month old white male developed a dry seborrhea capitis at approximately 6 weeks after birth which covered the whole scalp. Concomitantly, there was a severe seborrheic eczema of the face and body. By the time of examination, the child had been treated with various detergent ointment and lotion preparations without apparent effect. Soropon-pediatric solution was applied as a shampoo, directly to the scalp to remove the encrustations. Repeated applications were necessary for complete removal. Since the scalp was inordinately dry, lanolin cream was prescribed as a topical application after each shampoo. A series of 5 treatments were required for complete removal and after this treatment period the seborrheic eczema of the face and body had virtually disappeared. The patient was symptom free for the past three months.

There were no local tissue reactions, despite the fact that removal of the scales often left a raw surface exposed. There was no evidence of skin infection nor any exacerbation of an allergic reaction; in fact, when an allergic eczema existed concomitantly with the seborrhea capitis, its course often slowed and symptoms regressed as the scalp cleared. Repeated applications caused no sensitivity reactions.

Because of the difficulties involved in shampooing the heads of infants there were cases where the lather was inadvertently introduced into the eye. In none of these cases were there any instances of conjunctivitis, blepharitis or other ocular irritation.

The test preparation was evaluated for mucous membrane and eye irritation in rabbits by the procedure described by Draize and Kelley[5] which is based on the Draize, Woodard and Calvery method.[6] Three groups of three rabbits each were used; in the first group the test preparation was instilled into the eye of the rabbit and no further treatment instituted; in the second group, the preparation was instilled into the eye of the rabbit and flushed with 20 mm. of warm water, two seconds after treatment; in the third group, the preparation was instilled into the eye of the rabbit and flushed with 20 mm. of warm water, four seconds after treatment. The degree of reaction was noted at four hours after treatment and at daily intervals thereafter for seven days and was

SUMMARY OF RESULTS WITH FORTY-EIGHT PATIENTS TABLE II.

		Type of Seborrheic Capitis	Duration of Disease	Previous Medication	Concomitant Skin Diseases or Allergies	Maintenance Treatment	Results: Effective	Results: Non-Effective
SIX MONTHS OF AGE OR YOUNGER	Moderate [1]	Dry 23 cases Moist 1 case	2 weeks to 4 months	soap/water, Vioform ointment, 1%, oils, antibiotics, hydrocortone ointment, 1%, Mulsoy diet	urticaria, diaper rash, intertrigo, thrush, eczema of face, pyoderma, facial seborrhea, dermatitis, carbuncles, pustules, asthmatic bronchitis, atopic eczema	weekly, bi-weekly, p.r.n.	24 cases	0 cases
	Extensive [2]	Dry-7 cases Moist-4 cases Dry, scaly 1 case	3 weeks to 2 months	oils, Vioform ointment, 1%, hydrocortone ointment, 1%	corumenosis, eczema of face, arms, legs and neck, intertrigo, diaper rash, allergic	weekly, bi weekly, p.r.n.	12 cases	0 cases
OVER SIX MONTHS OF AGE	Moderate [1]	Dry 4 cases Fine 1 case	2 weeks to 3 months	antibiotics, hydrocortone ointment, 1%	facial eczema, allergic eczema, eczema	weekly, bi-weekly, p.r.n.	5 cases	0 cases
	Extensive [2]	Dry 4 cases Oily 1 case Dry, scaly 2 cases	2 months to 16 years	Vioform ointment, 1%, hydrocortone ointment, 1%, antibiotics, lanolin cream	corumenosis, eczema, asthmatic bronchitis, intertrigo, seborrheal dermatitis of scalp and body, hypothyroidism	weekly, bi- and tri weekly, p.r.n.	7 cases	0 cases

1- Moderate Scalp Involvement -small patches to one half of the scalp.
2- Extensive Scalp Involvement -more than one half of the scalp and, in some instances, the eyebrows.

scored according to the procedure of Draize and Kelley[5] with a maximum possible score of 110. From the results presented in Table II, it is apparent that a slight transient local reaction is observed which is of no clinical consequence. The maximum effect was noted four hours after exposure, and it is of interest to note that the third group (receiving palliative treatment) showed a greater response than the first group without palliative treatment. It might be well to consider the influence of the mechanical handling of this test when evaluating the responses observed. The effects noted in animals confirm the lack of irritation observed clinically. The material tested represents the undiluted therapeutic agent whereas under the conditions of clinical practice this material would have been diluted with water at the time of application to the wet scalp, further modifying any potential irritation.

COMMENT

Basically, seborrheic dermatitis, whether it occurs over the entire body or on the scalp alone, has the same etiological components. A hypersecretion of sebum, improperly removed, results in chemical decomposition of the exudate, and subsequent microbial infection of this seborrheic substrate usually develops into a seborrheic dermatitis. In time the skin may become sensitized to the infectious agent and vesiculation, pulstulation, oozing, and crusting follow. Seborrheic dermatitis of the body in general often starts in its milder form as a scaling of the scalp,[4] first as an intertriginous involvement of the skin folds and then extending to the face, neck, shoulders and trunk. This accentuates the importance of arresting the initial infectious state. Four of the eight typical cases presented in Table I showed additional seborrheic involvement which cleared as the seborrhea capitis regressed. The eminent correctness of primary symptomatic treatment thus becomes quite evident. Maintaining the scalp in a sebum-free condition lessens the infectivity and sensitivity, permitting the scalp to heal and present its natural protective surface to the invading organisms. The underlying problem, the total seborrheic diathesis, can then be attacked.

SUMMARY AND CONCLUSIONS

Forty-eight cases of stubborn "cradle cap" (seborrhea capitis infantum) were treated with a new antiseborrheic designed specifically for the dissolution of crusts and scales and for the cleansing of the scalp. The preparation was completely effective in every case.

The excellent results obtained with Soropon, combined with the unusually high safety factor and the lack of local irritation or sensitivity, seem to indicate that it is surely the therapy of choice in any seborrheic involvement, whether of the scalp or body

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CONGENITAL MIDGUT VOLVULUS

Case Report With Autopsy

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Congenital midgut volvulus causing neonatal death is rare. Gross[1] observed 156 cases of intestinal obstruction from malrotation of the intestines and colon and although one fourth of these were in infants under one week of age, none were noted to be present at birth.

CASE REPORT

The patient was a full term, female infant delivered from a 21 year old Negro woman, (Gravida III, Para I, Stillbirths O, Abortions 1). Birth weight was 3.17 kg. The mother's blood was type B, Rh positive. Her serology was negative. Delivery was accomplished under pudendal block with Trilene® anesthesia. The infant had a markedly distended abdomen at birth. Resuscitation using intermittent positive pressure oxygen was required for two minutes before respirations were established. The baby's general tone and condition remained poor. About thirty minutes after birth she became apneic and cyanotic and died a few minutes later.

AUTOPSY FINDING

Two areas of bluish discoloration were noted in the skin of the distended abdomen. One extended from the epigastrium to the left lower quadrant, the other was localized about the umbilicus.

The abdominal cavity contained hemolyzed and clotted blood. A dilated necrotic segment of small intestine filled most of the peritoneal cavity. Part of this infarcted small intestine was adherent to the inferior surface of the liver and part to the anterior abdominal wall in the right lower quadrant. This was found to be a volvulus of the small intestine associated with incomplete rotation of the bowel. The proximal small intestine was dilated and contained a green fluid material. The distal small intestine was partly filled with meconium.

* From the Department of Pediatrics, DeWitt Army Hospital, Fort Belvoir, Virginia.

Microscopic examination of the involved intestine showed necrosis and leukocytic infiltration, especially of the mucosa.

SUMMARY

A case of midgut volvulus secondary to malrotation of the bowel that developed in utero and caused death in the immediate neonatal period is presented.

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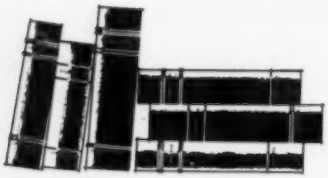
Blood factors Rh^A, Rh^B, and Rh^C occur associated with blood factor Rh_0 in Rh-positive blood. Occasionally, Rh-positive persons exist with blood lacking one or more of the factors Rh^A, Rh^B, and Rh^C and can become sensitized to the missing factor or factors, with resulting hemolytic transfusion reactions or infants with erythroblastosis. These cases produce the seeming paradox of an Rh_0-positive person with antibodies in his serum seemingly identical with anti-Rh_0 in specificity. Knowledge of the existence of blood factors Rh^A, Rh^B, and Rh^C will, therefore, aid the clinician in solving certain puzzling clinical problems relating to blood transfusion reactions and erythroblastosis fetalis.

With the aid of diagrams to help visualize the nature of the reactions of anti-Rh^A, anti-Rh^B, and anti-Rh^C, it is possible to anticipate the discovery of hitherto undescribed antibodies and blood factors. The diagrams also aid in clarifying certain previously observed relationships among blood factors in the Rh-Hr system, as well as in studies on the B and C blood group systems in cattle, serotyping of Salmonella bacteria, and the problem of so-called hybrid factors in the red blood cells of crosses between different species of pigeons and doves.

The Rh-Hr agglutinogen molecule of human blood might have two major side chains or combining sites, one for anti-Rh_0 and the associated anti-bodies anti-Rh^A, anti-Rh^B, and anti-Rh^C and the other for antibodies against the factor pairs rh′ and hr′, rh″ and hr″, and the related blood factors hr, rh_1, etc.

AUTHOR'S SUMMARY



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Edited by

MICHAEL A. BRESCIA, M.D.

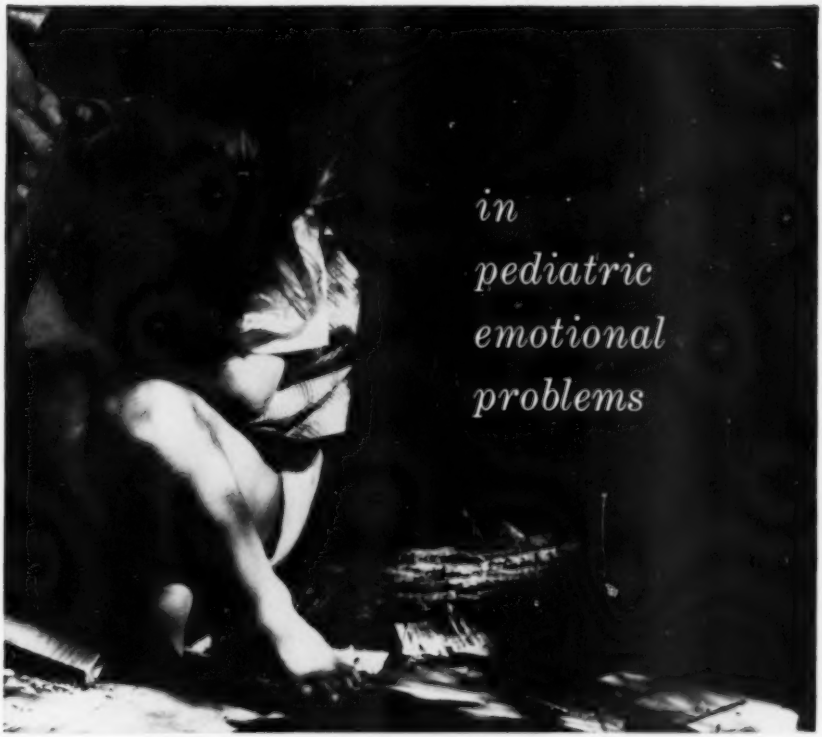
CLINICAL EPIDEMIOLOGY: By JOHN R. PAUL, M.D., pages 290 cloth, The University of Chicago Press, Chicago, Illinois, 1958 Price $5.00.

The purpose of this book is to apply a new philosophy to old diseases. The author points out the fallacies of the orthodox concept that epidemiology is the study of epidemics and therefore belongs wholly in the public health field. In contrast, Dr. Paul defines clinical epidemiology as the study of the ecology of disease and implies those aspects of this study which are of most immediate interest and use to physicians.

The author is concerned with the circumstances under which diseases occur, where diseases tend to flourish and where they do not. Such circumstances may be micro-biological or toxicological; they may be based on genetic, social, or environmental factors; even religious or political factors may come under scrutiny, provided they are found to have some bearing upon disease prevalence. The book goes beyond the study of epidemics, beyond infectious disease, and really deals with the milieu in which diseases grow. It soon becomes apparent that all diseases, all human blights and injuries have their epidemiology—cancer, benzol poisoning, alcoholism, drug addiction, suicides, automobile accidents, etc. That coronary thrombosis, rheumatic fever and infectious or serum hepatitis are events which demand epidemiological thinking and analysis on the part of the physician. The author cogently states that epidemiology thus helps to complete the clinical picture and the natural history of disease.

The book comprises twenty-one (21) chapters, covering a history, concepts of etiology, host susceptibility, serological epidemiology, environment, rheumatic fever, coronary occlusion, poliomyelitis, infections and serum hepatitis and arthropod-borne virus infestions.

Clinical epidemiology is a medical presentation rather than a strictly statistical or sociological point of view. I recommend this book as indispensable for physicians, medical students, interns, biologists, ecologists, public health officials, welfare workers and social workers. JOSEPH M. COVELLI, M.D.



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